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BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 15 1955

LUNG CANCER DEATH RATES AMONG NON-SMOKERS AND PIPE AND CIGARETTE SMOKERS

AN EVALUATION IN RELATION TO AIR POLLUTION BY BENZPYRENE AND OTHER SUBSTANCES

BY

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The rapid increase in death rates from lung cancer during the last twenty years has led to a search for possible environmental causes, and two sources of carcinogenic material have been suggested—namely, cigarette smoke and the smoke present in the atmosphere. The data so far accumulated from independent sources concerning these factors have suggested that each contributes in some way to the initiation of cancer of the lung and bronchus.

In 1947 the Medical Research Council planned a statistical study of smoking habits in this connexion, and the evidence which appeared three years later (Doll and Hill, 1950) showed a pronounced statistical association between smoking and lung cancer. This was substantiated by similar evidence from the United States of America (Wynder and Graham, 1950) and other countries, and a considerable literature has resulted. The statistical evidence received support by the isolation of a carcinogen, 3 : 4-benzpyrene, from cigarette smoke (Cooper, Lindsey, and Waller, 1954; Cooper and Lindsey, 1955; Seelkopf, 1955), and the production of tumours in mice by using a cigarette-smoke condensate has been reported (Wynder *et al.*, 1953). Nevertheless it has always been obvious that smoking could not account for all cases of lung cancer, though it has not been possible to make a reliable assessment of the proportion so caused.

Meanwhile a number of workers had demonstrated the differences between death rates in town and country (Stocks, 1936, 1939, 1947, 1952, 1955; Kennaway and Kennaway, 1947; Curwen, Kennaway, and Kennaway, 1954), and in 1947 one of us suggested that "either smokiness of the atmosphere is an important factor in itself in producing cancer of the lung, or sunshine is an important factor in preventing its incidence." Following closely upon these observations came reports of the detection of benzpyrene in domestic soot (Goulden and Tipler, 1949) and later in samples of atmospheric smoke (Waller, 1952; Cooper, 1954), but so far the data available for comparison of the benzpyrene content of town and country air have been scanty. In 1954, however, an apparent relationship was demonstrated between the carbon content of lungs and duration of life in large towns (Blacklock, Kennaway, Lewis, and Urquhart, 1954).

In this paper an attempt has been made to evaluate the effects of tobacco smoking and air pollution by benzpyrene acting together upon the male population of a particular region presenting great contrasts in respect of urbanization and smoking habits. It is an interim communication, and the conclusions to which it points are in no sense final, but the reasons for issuing it now are explained.

Sources of Data for Present Study

In 1952 the Cheshire and North Wales Branch of the British Empire Cancer Campaign, with the most helpful co-operation of the Medical Officers of Health and Regional Hospital Boards concerned and of the Clinical and Pathological Register for Cancer in the Liverpool Region, began to collect the past environmental histories of residents in North Wales and Liverpool Hospital Region who were diagnosed as suffering from, or certified as dying with, any form of malignant neoplasm. Starting from July 1 of that year, notifications have been received in respect of the deaths, and if no history has been obtained during life it is sought from near relatives through the agency of the medical officers of health and their health visitors. Supplementary information regarding the basis of diagnosis and duration of symptoms is sought from the certifying doctor, or from the records of the clinical register or hospital if there had been a hospital admission, and all records relating to an individual are brought together by means of a card index. The environmental history is taken on a standard schedule covering residences, occupations, work-places, travel to work, sources of water, milk, and vegetables, diet, methods of heating, cooking, and lighting, and other matters over a period of 20 years prior to the onset of symptoms. Full information is sought also on tobacco smoking and the marital history throughout the whole of life. During the first two years of the inquiry some 10,000 deaths of residents in the area, which were considered to be due to or to have been associated with cancer, occurred, and environmental histories were obtained in respect of about 90%.

*Operating from Westminster Chambers, St. Werburgh Street, Chester.

†Working under a grant from the Medical Research Council.

Starting early in 1953, precisely the same questions were asked of adult patients admitted to the hospitals at Bangor, Llandudno, Wrexham, and Chester, and to Broadgreen Hospital in Liverpool, this being done as a matter of regular routine by whole-time recorders appointed to the hospital staffs. The aim was to obtain, so far as possible, an environmental history from every adult in-patient regardless of cause of admission, so as to provide an unselected series of men and women who were not suffering from any form of cancer at any desired age, in addition to the histories of the cancer patients. When time did not permit of every patient without cancer being questioned, those omitted were not selected in any way which could introduce a bias in respect of past history. In the first two years some 12,000 histories, including tobacco smoking, were obtained from patients without cancer by this procedure. It is not known, and cannot be ascertained, to what extent, if at all, in-patients at general hospitals differ in respect of their past smoking habits from the whole population of the same age in the area served by the hospital. For some diseases some hospital bias doubtless exists, but for patients without cancer *in toto*, even if such bias is appreciable, it may be assumed to be of the same kind in different general hospitals. Consequently it should not affect the conclusions drawn in this study, which depend upon comparative rather than absolute estimates of the distributions of smokers and non-smokers in the areas served by the hospitals. Knowing the census populations of these areas by sex and age, and the proportions at each age in various smoking categories, the actual populations in those categories can be estimated.

In 1954 arrangements were made with the Medical Research Council and Department of Scientific and Industrial Research for the supply and installation of 10 air filters of a new design at 10 places in the research area and for analyses in respect of total smoke, trace elements, 3 : 4-benzpyrene, and other polycyclic hydrocarbons contained in the air. The filters are provided by the Fuel Research Station at East Greenwich, and are located usually at health offices, the weekly change of filter papers and reading of the air-meter being carried out by those who are kindly housing the instruments. From October 13, 1954, the filters worked continuously, apart from an occasional breakdown, and analyses for the first six months have by now been made of total smoke at the Fuel Research Station, and of the hydrocarbons at the Pathological Department of St. Bartholomew's Hospital by one of us (J. M. C.). Monthly measurements of sulphur dioxide in the air at the same places are being made by lead peroxide cylinders provided by the Department of Scientific and Industrial Research, the analyses being carried out by the city analyst at Liverpool.

Purpose of this Preliminary Report

The purposes of this paper are : (1) to compare the death rates from lung cancer in the two-year period from mid-1952 to mid-1954 amongst men between the ages of 45 and 75 who had been non-smokers, pipe smokers, light, moderate, and heavy cigarette smokers, and who were resident in three areas differing greatly in respect of their urbanization ; and (2) to report upon the atmospheric content of smoke, sulphur dioxide, 3 : 4-benzpyrene and certain other polycyclic hydrocarbons during six months from October, 1954, to April, 1955, at representative localities within the same three areas and also at some other places in the Merseyside and Deeside region. Such an evaluation is being made now instead of waiting for five-year death rates based on larger numbers, because the two-year rates for men seem to point strongly to certain conclusions which might conceivably help to hasten effective action towards reducing lung cancer incidence, and consequently it was considered that they ought to be put on record for the information of research workers in this field. Certainty about the causation of lung cancer is unlikely to result from any single research, whether chemical, experimental, clinical, or statistical ; most probably conclusions will have to be reached on the grounds of consistency between data and by piecing together evidence from diverse sources rather than by relying upon very high degrees of statistical significance in any one study. In this particular study the advantages of delaying any statement until the five-year survey has been completed might be that death rates of women can then also be examined, analysis by other factors such as occupations will be possible, some irregularities in the rates will probably disappear, and the statistical significance of differences may be enhanced. In circumstances where new evidence is urgently needed these advantages do not seem to justify delay, but it must be emphasized that the conclusions indicated in this interim communication are subject to possible modification in the final analysis.

Urban and Rural Smoking Habits

Men aged 45–74 who were admitted as in-patients and for whom no diagnosis of any form of malignant neoplasm was made before discharge provide the data for assessment of past smoking habits of three age groups, 45–54, 55–64, and 65–74, living in three areas surrounding the hospitals at (R) Bangor and Llandudno, (M) Wrexham and Chester, (U) Liverpool (Broadgreen Hospital). These areas, which offer great contrasts, were defined geographically as (R) the counties of Caernarvon and Anglesey, which are rural with no industrial towns ; (M) the county borough and rural district of Chester, urban and rural districts of Wrexham, urban districts of Wirral, Neston, and Hoole, and rural districts of Hawarden, Runcorn, and Tarvin, a mixed rural and urban area ; (U) the county borough of Liverpool, which is densely urban. The areas are shown on the map in Fig. 1. The

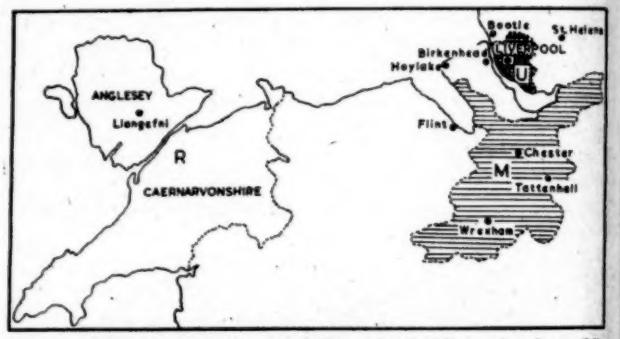


FIG. 1.—Map showing the rural (R), mixed (M), and urban (U) areas, and location of the ten air filters (●).

census populations of men aged 45–54, 55–64, and 65–74 in these areas have been divided into six smoking categories by applying the proportions amongst the non-cancer patients of those ages, whose totals seen at the relevant hospital centres were 802, 1,757, and 969 at ages 45–74 in the R, M, and U areas.

The record of tobacco smoking includes the average weekly number of cigarettes and ounces of pipe tobacco smoked during successive 10-year periods of age, with details also of cigars, tobacco chewing, use of petrol lighter, and ages at starting and ceasing for each of these. If a change took place from cigarette to pipe smoking or vice versa the assignment is to the one for which the weekly amount of tobacco was greatest, counting 25 cigarettes as equivalent to 1 oz. (28 g.) of pipe tobacco. If both cigarettes and pipe were smoked during the same period the assignment is to the cigarette category corresponding to the combined amount of tobacco. Pipe smokers therefore exclude true mixed smokers, and also all who had smoked cigarettes except those who had changed from one to the other with a greater weekly tobacco consumption during the pipe phase. The classification is based on the largest average weekly amount stated for any 10-year age period. Non-smokers are defined as those who have never for any period averaged as much as two cigarettes per week and have not smoked a pipe or cigars or been chewers of tobacco.

The categories used in this study have been condensed to five:

Non-smokers—as defined above
Pipe smokers—as defined above
Cigarette smokers:
Light—maximum 2–99 per week
Moderate—maximum 100–249 per week.
Heavy—maximum 250 or more per week

Table I shows the proportions in each category amongst the male non-cancer patients of each age group in areas R, M, and U, and Table II gives the corresponding populations of the areas estimated by applying those proportions to the census. It is evident from the first table that the urban area has the lowest proportions of non-smokers, pipe smokers, and light cigarette smokers, and the highest proportions of moderate and heavy cigarette smokers. Comparing the mixed with the rural area, the former has higher proportions of non-smokers, moderate and heavy cigarette smokers, and lower proportions of light cigarette smokers. Pipe smoking is much more frequent in the higher age groups in each area, and in the rural area 40% of men aged 65–74 fall into this category.

Urban and Rural Death Rates from Lung Cancer by Smoking Categories

Precisely the same information on past smoking habits was asked for in respect of all residents in the areas R, M, and U who died with cancer of the lung, bronchus, or pleura in the two-year period; and if no record had been obtained during life this was obtained whenever possible from the widow or other relative. Before relating the data thus collected to the population in Table II, two corrections are necessary. In some instances the desired information about smoking could not be obtained because of the failure to interview the relative, sometimes because none were known, sometimes on account of removal out of the research area, or, in rare instances, through refusal or inability to give the information. Since these causes of failure had no possible association with smoking habits and such cases comprised only 1 in 5 of the total, they were distributed over the four categories of smokers in the same proportions as the known cases. None were added to the non-smokers, that category including only persons concerning whom a definite statement had been made that they had never smoked. The second correction is for a tendency to understatement by the widow of the weekly number of cigarettes which had been smoked by her husband. The extent of this tendency was measured by comparing the records of 35 men who had been seen in hospital and had then died before the hospital record had been received and indexed, with the result that the second record was obtained from the widow. Every effort is made to avoid this occurring, but such dual records will be invaluable as data by which to test the consistency and reliability of information on different matters of environmental history. The first 35 cases showed the average weekly number of cigarettes to be 121 according to the men themselves and 106 according to their widows, and in order to correct for this understatement appropriate fractions of the light and moderate cigarette smoking categories were transferred to the next higher group. Table III gives the mean annual death rates obtained by dividing the corrected number of deaths in the two-year period by the corresponding population at risk in Table II and multiplying by 100,000. The rates are also represented pictorially in Fig. 2.

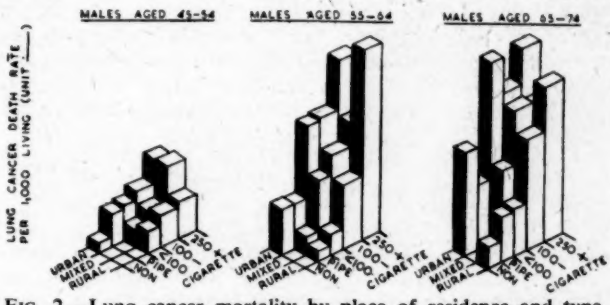


FIG. 2.—Lung cancer mortality by place of residence and type and amount of smoking.

In the rural area of Caernarvon and Anglesey the death rates increase progressively with weekly cigarette consumption at each age, and the standardized death rate (S.D.R.) when plotted on a scale of number of cigarettes forms almost a straight line, the increment of death rate being about 1 per 1,000 for each 13 cigarettes a day. For all pipe smokers the rate corresponds with that of smokers of 25 cigarettes per week, the equivalent of about 1 oz. (28 g.) of tobacco, whereas the average weight of tobacco reported to have been smoked by the group of pipe smokers was about 3 oz. (85 g.). This suggests that in this rural area pipe smoking is only one-third as dangerous as consuming the same amount of tobacco in the form of cigarettes.

In the mixed rural and urban area the death rates of light and moderate cigarette smokers, who there form two-thirds of the male population at ages 45–74, are higher than in the rural area, but this is not true for heavy smokers, nor for pipe smokers aged 65–74.

TABLE I.—*Percentage Distributions According to Past Smoking Habits Among Male Hospital In-patients Without Cancer in Rural, Mixed, and Urban Areas*

Smoking Category	Ages 45–54			Ages 55–64			Ages 65–74		
	Rural	Mixed	Urban	Rural	Mixed	Urban	Rural	Mixed	Urban
Non-smokers	5·9	10·8	3 5	9·9	9 9	4·2	10·2	17·7	3 8
Pipe smokers	9·9	8·5	2 3	16·7	15 8	11·1	43·7	30·1	16·6
Cigarette:									
Light	35·9	26·7	18·4	33·7	29·0	16·7	27·1	21·9	21·0
Moderate	43·9	48·2	65·1	34·9	37·5	57·8	18·6	26·4	50·0
Heavy	4·4	5·7	10 7	4·8	7·8	10·2	3·4	3 9	8·6
Total	100	100	100	100	100	100	100	100	100

TABLE II.—*Estimated Populations of Men of Different Smoking Habits at Risk in Two Years, in Three Regions—Rural, Mixed, and Urban*

Smoking Category	Ages 45–54			Ages 55–64			Ages 65–74		
	Rural	Mixed	Urban	Rural	Mixed	Urban	Rural	Mixed	Urban
Non-smokers	1,351	4,183	3,181	1,897	2,645	2,711	1,417	3,146	1,487
Pipe smokers	2,280	3,327	2,114	3,186	4,232	7,042	5,667	5,352	6,591
Cigarette:									
Light	8,296	10,298	16,751	6,450	7,771	10,665	3,778	3,897	8,292
Moderate	10,135	18,618	59,339	6,679	10,046	36,862	2,598	4,694	19,766
Heavy	1,012	2,202	9,751	910	2,074	6,506	474	703	3,400
Total	23,054	38,628	91,136	19,122	26,768	63,786	13,934	17,792	39,538

TABLE III.—*Lung Cancer Death Rates (mean annual per 100,000 from mid-1952 to mid-1954) of Men in Rural, Mixed, and Urban Areas Classified According to past Smoking Habits*

Smoking Category	Ages 45–54			Ages 55–64			Ages 65–74			S.D.R. 54–74*		
	Rural	Mixed	Urban	Rural	Mixed	Urban	Rural	Mixed	Urban	Rural	Mixed	Urban
Non-smokers	0	0	31	0	0	147	70	0	336	14	0	131
Pipe smokers	0	0	104	34	59	143	145	26	232	41	25	143
Cigarette:												
Light	69	57	112	70	224	378	154	259	592	87	153	297
Moderate	90	83	138	205	285	386	362	435	473	183	132	287
Heavy	117	214	205	626	362	543	506	412	588	363	303	394
No. of deaths	16	26	124	25	56	232	27	36	183	68	118	539

* Standardized rate based on Liverpool population.

In Liverpool the rates exceeded those in the rural and mixed areas for every group, but the gradient of death rate with rising cigarette consumption is not as steep as in the rural area, nor is it as regular, probably owing to some amount of misfit between the hospital population and deaths. The ratio of rural to urban S.D.R., expressed as a percentage, increases as follows from non-smokers to heavy cigarette smokers:

Non-smokers	11
(Pipe smokers)	(29)
Light cigarette smokers	29
Moderate " "	64
Heavy " "	92

This result disposes of the possibility that the urban excess of lung cancer could arise merely from more complete recognition of the disease in towns combined with differences in smoking habits of the populations, since in that event there would be no reason why the ratio should differ according to smoking category. The urban/rural ratio of 9 to 1 for non-smokers is founded on small numbers, and would be subject to a considerable standard error had it not been supported by the trend of the other ratios. Comparing the rates for the three cigarette categories with the weekly numbers of cigarettes, which average about 310, 150, and 62 in the heavy, moderate, and light categories, the percentage rural/urban ratios are 92, 64, and 29, and from these figures, which are based on larger numbers, it is reasonable to expect a ratio about 14% at the zero point.

The differences between the urban and rural standardized death rates are 117 for non-smokers, 102 for pipe smokers, and 104 for moderate cigarette smokers, and this suggests that the Liverpool environment exposes men to a carcinogen which adds about 100 to the death rate per 100,000 from lung cancer, whether they smoke or not, the increment being possibly rather less for heavy cigarette smokers, though that is doubtful. This could happen if urban air contains a carcinogen, which could be the same or different from the one derived from cigarette smoking. In that case it would be expected that the ratio between the urban and rural concentrations of the agent in the air would be about the same as the ratio between the urban and rural death rates among non-smokers, since the average amount inspired in a given time must be proportional to the concentration in the air and the cases of cancer resulting from it would also increase with the concentration.

It may be noted here that, by collecting the smoke produced by mechanical smoking of cigarettes, Cooper and Lindsey (1955) have found that 500 cigarettes produce 4 μg. of 3:4-benzpyrene. On this basis the group of light cigarette smokers as defined in this study will, with an average of 62 cigarettes per week, be taking in about 26 μg. per year through smoking, the moderate group (average 150 per week) about 62 μg. and the heavy smokers (average 310 per week) about 130 μg. The mean cigarette consumption in populations of men of the three age groups was 80 per head per week in area A, 88 in area M, and 126 in area U; and the average intake of benzpyrene through smoking on this basis would be 33 μg. per annum in Anglesey and Caernarvonshire, 37 in the mixed area, and 52 in Liverpool. The deaths from lung cancer at the same ages were 1.3, 1.5, and 2.7 per 1,000 in those areas, and this suggests that if benzpyrene is the carcinogen concerned the differences in smoking habits would account for about half of the urban-rural differences in the lung cancer rates. The further possible significance of these figures is discussed in the section on "combined intake."

Contributions of Smoking and "Urban" Factor to the Deaths in Liverpool

By applying the various death rates according to age and smoking category in Table III to the estimated populations at risk in Liverpool, the following totals of deaths from cancer of the lung, bronchus, and pleura would have resulted in the two-year period on different assumptions:

Number of lung cancer deaths among men aged 45–74 in Liverpool in two years from mid-1952 to mid-1954	539
If death rates in each smoking category were to remain as in Liverpool and:	
Smoking habits as in rural area	481
All had been non-smokers	256
" " " pipe smokers	271
" " " light cigarette smokers	550
" " " heavy " "	769
If death rates in each category were as in the rural area and:	
Smoking habits as in Liverpool	315
" " " " rural area	221
If death rates were as in non-cigarette smokers living in the rural area	63

According to this, abolition of cigarette smoking might be expected eventually to reduce the deaths of men in Liverpool from lung cancer by about one-half, and three-quarters of the remaining half would be due to some local cause only slightly present in the rural area and most likely to be some kind of air pollution.

Chemical Analysis of Suspended Impurity in Rural and Urban Air

The object of the chemical investigation was to determine the concentration of the carcinogen 3:4-benzpyrene and other polycyclic hydrocarbons in the suspended impurity of the air at places in North Wales, Cheshire, and Merseyside. This impurity consists of ash, smoke from chimneys and vehicular exhausts, and other windborne dust. The amount of pollution caused by this material suspended in the atmosphere depends on the amount of industry and the number of houses in the area concerned; so sampling stations were set up at 10 sites where very different levels of pollution might be expected. The amounts of hydrocarbons contained in the impurity were extremely small, and spectrophotometry had to be used to identify and determine individual compounds. Anthracene, pyrene, fluoranthene, 3:4-benzpyrene, and 1:12-benzperylene were determined quantitatively in all samples.

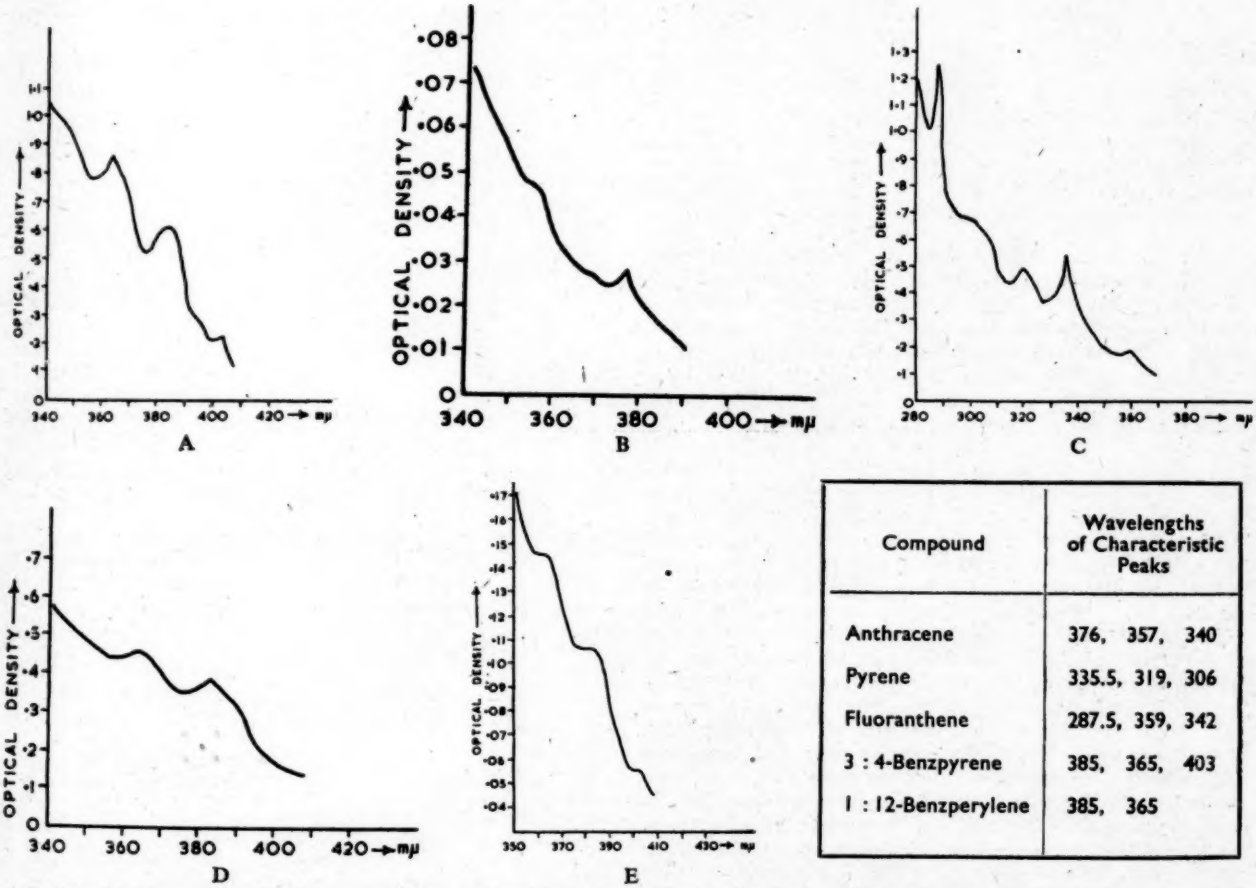
The following analytical technique was used. At each of the 10 sites chosen air was drawn continuously, night and day, through a glass tube leading from outside the building to a Whatman No. 1 filter paper inside the building, at a rate of about 50 cubic feet (1.41 cubic metres) a day. The filter paper was fitted to either a 2-in. (5-cm.) or 4-in. (10-cm.) holder which was connected to an electrically operated pump through a gas-meter, the 4-in. holder being used in large towns and the smaller holder in country districts. At each place the papers were changed weekly, and at the same time the volume of air which had passed through the filter was read from the gas-meter. Each paper had a dark stain caused by the arrested impurity, varying in colour from light grey to black. The weight of material

on each paper was determined at the Fuel Research Station at East Greenwich, either visually by comparing with Owen's standard scale or photometrically by measuring the intensity of reflected light with a standardized photo-electric cell and galvanometer. Both methods have been standardized by direct weighing, so that the weight corresponding with a given shade reading is known. (Department of Scientific and Industrial Research, 1945.)

The filter papers were then cut in halves, one-half being kept for trace-element analysis. The other halves were extracted in a Soxhlet apparatus with acetone until no more fluorescent material was washed out, a process taking about three hours. The acetone was boiled off gently and the residue taken up in cyclohexane, and this solution was chromatographed on a standardized column of alumina, using cyclohexane as an eluent initially and later adding increasing concentrations of benzene. Fractions of about 3 ml. were collected, and each was examined by means of a Unicam S.P.500 spectrophotometer. From a previous study of artificial mixtures, the order in which the hydrocarbons were eluted from the column was known, so each fraction could be examined for the appropriate hydrocarbons by the method of searching for peaks (Wedgwood and Cooper, 1953). Fractions containing individual hydrocarbons were combined and the concentration of each hydrocarbon was determined spectrophotometrically. Finally, the spectrophotometric readings were converted into weights of hydrocarbon and these values expressed as parts per million of deposit and as micrograms per 100 cubic metres of air (μg./100 cubic metres). All glass apparatus used was cleaned in chromic-sulphuric acid mixture and rinsed with cyclohexane, and all solvents used were redistilled twice and residues examined. The alumina was also extracted with cyclohexane and examined after use, and finally a complete experiment was run with blank filter papers. All these tests showed the absence of hydrocarbons in the materials used in the analyses, but the filter papers contained the following weights of compounds expressed as μg. per half-paper: pyrene, 0.003; fluoranthene, 0.002; benzpyrene, 0.004; giving a possible error of less than 3%.

The weights of deposit on the filter papers were found to differ widely according to the locality; for example, in the first week of operation of the filters in October the amounts at five places were as follows: Llangefni, 0.180; Hoylake, 0.327; Flint, 0.721; St. Helens, 1.704; Liverpool, 3.212 mg. There was also considerable variation from week to week in the same locality as well as seasonal change; for example, the amounts of deposit in mg. per cubic metre of air at Liverpool during four weeks from October 13 to November 10 were 0.350, 0.382, 0.522, 0.523, and the six 4-week averages between October 13 and March 30 were 0.413, 0.497, 0.412, 0.342, 0.270, 0.261. Daily and weekly meteorological measurements are being recorded at each filter station for eventual correlation with the analyses.

It was found impracticable to work with less than 5 mg. of the deposit, and consequently, in order to have sufficient material for analysis from the less-polluted areas and to obtain an average value for each locality, the weekly papers were extracted together as follows: for Llangefni, Tattenhall, Chester, Wrexham, Flint, and Hoylake, 13 weeks at a time, and for Liverpool, Bootle, Birkenhead, and St. Helens four weeks at a time. This made 36 estimations in all for the half-year and yielded total deposits ranging from 5.4 mg. in 13 weeks at Llangefni to 24 mg. in 4 weeks at Liverpool. The extracts were each made up to 10 ml., sufficient being then taken to provide an extract representing about 5 mg. of deposit. In this way the chromatographic procedure could be standardized to give identical conditions for each separation.



Compound	Wavelengths of Characteristic Peaks
Anthracene	376, 357, 340
Pyrene	335.5, 319, 306
Fluoranthene	287.5, 359, 342
3 : 4-Benzpyrene	385, 365, 403
1 : 12-Benzperylene	385, 365

FIG. 3.—Spectra of 3:4-benzpyrene and other polycyclic hydrocarbons. (A) Spectrum of 3:4-benzpyrene for combined extracts, showing characteristic peaks. (B) Spectrum of anthracene for combined extracts. (C) Spectrum of pyrene and fluoranthene for combined extracts. (D) Spectrum of 1:12-benzperylene for combined extracts. (E) Spectrum of 3:4-benzpyrene for Birkenhead, weeks 13–16, showing inflexions.

With such small quantities of material, the only means of identification were inflexions at the correct positions in the spectrum, as shown in Fig. 3. When the concentration is increased the inflexions become the peaks of the characteristic spectrum, and to furnish evidence for their identification the fractions containing the separated hydrocarbons from each estimation were combined at the end, concentrated, and the spectrum plotted (see spectra). Finally, the solutions containing these individual hydrocarbons have been kept, and it is hoped to brominate the fractions so that the characteristic spectra of the brominated hydrocarbons may provide further evidence for the identification of each compound (Cooper, Goldup, and Lindsey, 1955).

The results are shown in Table IV in the form of average weights of total smoke and of the hydrocarbons per 100 cubic metres of air during six months, starting from mid-October. Sulphur dioxide indices, obtained by lead peroxide candles exposed in louvered boxes located near to the intake tubes of the air filters, are also included in the table.

TABLE IV.—*Average Concentrations of Smoke, Benzpyrene, Other Polycyclic Hydrocarbons, and Sulphur Dioxide at 10 Localities During Six Months from October 13, 1954*

Location of Filter (See Fig. 2)	Total Smoke (1)	3:4-Benzpyrene (2)	1:12-Benzperylene (2)	Pyrene (2)	Fluoranthene (2)	Anthracene (2)	SO_2 (3)
Areas for this study:							
Rural:							
Llangefni ..	4·9	0·7	0·7	0·3	0·5	0·1	0·3
Mixed:							
Tattenhall(rural)	6·4	1·0	0·9	0·5	0·6	—	0·4
Chester (urban)	21·8	1·9	5·3	0·7	1·5	—	1·1
Wrexham ,,	23·3	5·1	1·8	1·2	1·4	0·4	1·1
Urban: Liverpool	36·3	7·7	6·6	2·3	2·4	0·7	2·8
Urban/rural ratios:							
Liverpool/ Llangefni ..	*7*	*11*	*9*	*7*	*5*	—	*8*
Liverpool/ Tattenhall ..	*6*	*8*	*7*	*5*	*4*	—	*7*
Other localities:							
Flint	15·2	3·3	2·1	0·9	2·2	0·1	0·8
Hoylake ..	10·0	2·8	1·7	0·7	0·9	0·1	0·9
Birkenhead ..	28·4	5·8	4·9	2·8	3·9	0·5	1·8
Bootle	34·2	8·5	4·1	3·7	4·9	0·9	2·3
St. Helens ..	37·3	7·7	5·3	3·1	3·9	1·2	2·6

Notes.—(1) In mg. per 100 cubic metres; averages for 26 weeks. (2) In μg. per 100 cubic metres; averages for 24 weeks at Liverpool, Birkenhead, Bootle, St. Helens; 26 weeks elsewhere. (3) In mg. of SO_2 per day collected by 100 sq. cm. of lead peroxide during four months, March to June.

The first five stations are located in the rural, mixed, and urban areas used in Tables I–III, and the places were chosen as apparently representative of average conditions in those areas. Llangefni and Tattenhall are of a rural character, Chester and Wrexham are towns of moderate size in fairly open country, though the latter has coal mines in its vicinity, and the Liverpool filter is in the middle of a large densely populated conurbation. The concentrations are seen to rise with increasing urbanization and population density, the only notable irregularity being the contrast between the benzpyrene and benzperylene figures for Chester and Wrexham. For total smoke and pyrene the Liverpool concentrations are about six times as great as in the rural localities, for 3:4-benzpyrene the ratio is around 10 to 1, and for 1:12-benzperylene and sulphur dioxide the ratios are about 8 to 1. These are interesting in view of the 9 to 1 ratio for lung cancer death rates amongst male non-smokers in the urban and rural areas and the known carcinogenic properties of benzpyrene. The benzpyrene content of the smoke deposit in parts per million of the total solid matter showed little excess in Liverpool in comparison with the rural areas, the average figure in six months being 187 p.p.m., compared with 150 at Llangefni and 155 at Tattenhall, but that does not affect the hypothesis that benzpyrene may be the important agent, since it is the total intake of the hydrocarbon which would be expected to show a proportionality with the death rate. Since 1:12-benzperylene is suspected to have weak carcinogenic properties its possible agency should not be overlooked, but there is no good reason at present for suspecting the other substances. It has been found, however, that exhaust fumes from diesel engines, when operating inefficiently or accelerating, contain considerable amounts of benzpyrene, benzperylene, and pyrene, and that the mixture is capable of producing skin cancers in mice (Kotin, Falk, and Thomas, 1955).

Although current death rates have not yet been ascertained for the other places in Table IV, the comparative mortality ratios of males for lung cancer in 1947–51, standardized on the North Wales population, were as follows: Bootle, 289; Liverpool, 238; Birkenhead, 187; St. Helens, 173. For the first three of these towns the benzpyrene concentrations of 8.5, 7.7, and 5.8 show some correspondence, but the St. Helens figure of 7.7 would lead to the expectation of a higher rate than was observed in those years. It must be borne in mind, however, that present smoke analyses will sometimes fail to indicate correctly the relative conditions in towns 10 to 20 years ago which led to changes in the lung now producing deaths.

Combined Intake of Benzpyrene from Air and Smoking

From Cooper and Lindsey's finding that 4 μg. of 3:4-benzpyrene can be extracted from the smoke of 500 cigarettes, together with the amounts of that substance in air as determined by almost the same technique and given in Table IV, it is possible to estimate what would be the total intake per year by men of different smoking categories living in the rural and urban areas on various assumptions regarding the amount which actually reaches the lungs. During normal respiration some filtration takes place in the nose, and this may prevent much of the suspended matter reaching the bronchi. Also, it is not known at present to what extent the air inside factories, offices, and houses contains the suspended matter present in the outside air with its complement of benzpyrene. During sleep in average housing conditions little suspended matter may be reaching the lungs, whereas in some dusty work-places the amount may be increased rather than reduced. All that can be done is to calculate the amount of benzpyrene inspired on the assumption that a man is breathing the outside air all the time, and that all of it is reaching the lungs; add trial fractions of this to the calculated intake from cigarettes, and then compare the results with the death rates from lung cancer. The figures in Table IV relate to the autumn and winter, and will be lower in spring and summer; so to correct for this the annual averages may be taken provisionally as four-fifths of these concentrations.

Taking the amount of air inspired by the "standard" man during working, resting, and sleeping as 7,300 cubic metres a year, the mean average intake of benzpyrene from the air on the maximum assumption would be: in the rural area (represented by Llangefni) about 41 μg., in the mixed area (average of Tattenhall, Chester, and Wrexham) about 157 μg., and in Liverpool about 450 μg. Table V shows the result of adding (1) one-fourth, and (2) one-twelfth, of these amounts to the estimated quantities derived from

TABLE V.—*Estimates of Combined Intake of Benzpyrene in a Year from Air and Cigarettes on Certain Assumptions*

	Assumption (1)				Assumption (2)				S.D.R.
	Rural	Mixed	Urban	Rural % of Urban	Rural	Mixed	Urban	Rural % of Urban	Rural % of Urban
Non-smokers	10·3	39	113	*9*	3·5	13	38	*9*	*11*
Cigarette smokers:									
Light ..	36	65	139	*26*	29	39	64	*46*	*29*
Moderate	72	101	175	*41*	65	75	100	*65*	*64*
Heavy..	140	169	243	*58*	133	143	168	*79*	*92*
All males 45–74	43	76	165	*26*	36	50	90	*40*	*41*
Ratio to urban%:									
Intake					*40*	*56*	*100*		
S.D.R.					*41*	*51*	*100*		

cigarette smoking by each group of men, and comparing the relative figures with the relative death rates from lung cancer.

The measure of agreement between the relative values of benzpyrene intake on assumption (2) and those for the standardized death rates (S.D.R.) in the various groups is such as to justify a working hypothesis that benzpyrene might be the agent responsible for the associations of lung cancer with both smoking and urban residence, and to encourage research into the amounts of this and other hydrocarbons in the air, both outside and inside buildings, in different localities.

Summary

By means of data from the first two years of the study of environmental histories of persons with and without cancer which is being carried out by the Cheshire and North Wales Branch of the British Empire Cancer Campaign, death rates from cancer of the lung and bronchus have been calculated amongst men of different smoking habits living in a rural area of Wales, in a mixed area around Chester and Wrexham, and in Liverpool county borough. The death rates have then been related to measurements of benzpyrene and other substances present in the air at various places within those areas.

The rural death rate increases proportionately to the number of cigarettes smoked per week, and pipe smokers as a group rank with cigarette smokers of about 25 a week. Liverpool rates exceed the rural rates in every smoking category, but the urban/rural ratio falls progressively from about 9 to 1 amongst non-smokers to a small value approaching unity amongst heavy cigarette smokers.

The absolute urban excess is much the same in each smoking group, suggesting that an "urban" factor is added to the effects of smoking. Differences in smoking habits of the populations can account for only a small fraction of the contrast in total rates, and it is estimated that about half the Liverpool deaths of men from lung cancer arise from cigarette smoking and about three-quarters of the remaining half are due to a factor which is only slightly present in the rural area.

The concentration of smoke and of 3 : 4-benzpyrene, other polycyclic hydrocarbons, and sulphur dioxide in the air rises with increasing urbanization, the benzpyrene figure in Liverpool being 8 to 11 times as great as in the rural localities examined, a ratio which corresponds with the estimated mortality ratio amongst non-smokers living in those areas. When the death rates are compared with the calculated total intake, by different categories of smokers in the areas, of benzpyrene derived from air according to certain assumptions, plus that derived from the number of cigarettes smoked, the degree of correspondence is such as to suggest that benzpyrene might be the one agent involved.

This interim communication is being made because a supposition that benzpyrene plays a dual part, through cigarettes and air pollution, now appears to be tenable, and such a working hypothesis may assist research work in this field whether or not it is finally substantiated.

In collecting the patients' histories on which this study is based many people have co-operated, and acknowledgment is made to the medical officers of health, doctors, and health visitors in the counties of Anglesey, Caernarvon, Denbigh, Flint, and Cheshire, and county boroughs of Liverpool and Chester; to the Management Committees of Bangor, Wrexham, Chester, and Broadgreen Hospitals; and to the patients and their relatives. For help with the installation and operation of the air filters our thanks are due to Dr. E. T. Wilkins and Mr. J. R. Goss, of the Fuel Research Station at East Greenwich, to the sanitary officers at the various stations, the N.H.S. Executive Council at Liverpool, and Dr. K. C. Kershaw at Tattenhall. Professor J. W. S. Blacklock and Sir Ernest Kennaway, of the Department of Pathology, St. Bartholomew's Hospital, the Medical Research Council, the Department of Scientific and Industrial Research, and the Clinical and Pathological Register for Cancer in Liverpool are also thanked for their help.

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TUBERCULOSIS IN STUDENTS AND NURSES

BY

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Six years have elapsed since the findings of the Prophit Survey on Tuberculosis (1948) in young adults was published; in that report the incidence and pathogenesis of the disease in medical students and nurses in the London area were reviewed. In the present paper we record the incidence of tuberculosis in students of all faculties of four representative universities during a three-year period and discuss the results of a B.C.G. vaccination programme in medical students and nurses of ten university centres. A comparable analysis of the tuberculosis problem in American medical schools and the results of B.C.G. vaccination there has been published by Abruzzi and Hummerl (1953), who reported an incidence of 3.34 per 1,000 per annum in medical students, compared with the 2.5 per 1,000 per annum of British students of all faculties. In relation to B.C.G. vaccination, three cases of clinical tuberculosis have occurred in each of the series of 4,400 American and 2,630 British vaccinated students.

Mass Radiography Survey

The miniature radiograph is our most potent weapon in the detection not only of the infectious student but also of the early pulmonary lesion.

Table I is an analysis of 43,431 examinations of students in the Universities of Edinburgh, Glasgow, Cambridge, and Belfast during the period 1950–3.

In Edinburgh in 1950–1 only first-year students were required to undergo *x*-ray examination; to the others it was optional, and, although every student was obliged to walk through the mass radiography unit to reach the matriculation office, and although each was invited to submit to the

Table I.—*Number of Students at Risk and Percentage Surveyed*

University	1950–1			1951–2			1952–3			Average
	No. Sts.	No. X-rays	%	No. Sts.	No. X-rays	%	No. Sts.	No. X-rays	%	
Edinburgh	6,300	2,795	43	6,040	5,142	85	5,850	4,898	83	71%
Glasgow	6,790	3,782	56	6,526	4,494	69	5,980	3,889	65	63%
Cambridge	5,395	3,848	70	6,040	3,965	65	6,000	3,445	57	64%
Belfast ..	2,633	2,368	82	2,614	2,263	86	2,557	2,381	93	87%

examination, only 43% took advantage of the offer. Much has been said concerning freedom of choice for students, but in matters of this kind direction and regulation appear to be the only practical methods of obtaining their co-operation.

In the past two years whole-time students in Edinburgh have been unable to matriculate until they produce an *x*-ray card or a letter of exemption from the secretary of the university. In this way, 84% of the total student population have been examined; the remainder comprise research, post-graduate, and part-time students, and those who matriculate at odd times in the year. In Edinburgh, therefore, an average of 71% have been examined.

In Glasgow all students are now required to undergo annual examination, and in the past three years an average of 63% have been reviewed.

In Cambridge all first-year students are examined and certain colleges encourage an annual re-examination for all students; so that 64% have been *x*-rayed.

In Belfast, where all whole-time undergraduates are examined annually, the average number scrutinized amounts to 87%, and is the highest in the series.

Incidence of Tuberculosis

It has been found practical and convenient to classify cases showing evidence of tuberculous infection into the four categories as adopted by Sir Alan Rook, of Cambridge: (A) old lesions requiring no further action; (B) previously diagnosed, but requiring observation; (C) newly discovered significant lesions—(1) requiring immediate treatment, (2) requiring further observation; (D) doubtful appearances requiring observation. The total possibly active cases comprise categories B and C together.

Category A represents old healed lesions, such as calcified primary foci or calcified parenchymal lesions and glands. Students in whom a diagnosis of pulmonary tuberculosis has been made before arrival at the university and who are under treatment or observation are placed in category B. Newly discovered lesions are classified further as those requiring immediate treatment for progressive lesions, and those showing a lesion of doubtful significance, such as a small primary focus. Category D includes findings intermediate between those of categories A and C (2).

Table II.—(*A*) *Old Lesions Requiring No Further Action*

University	1950–1	1951–2	1952–3	Incidence per 1,000
Edinburgh ..	17	22	19	3·2
Glasgow	54	47	169	14·0
Cambridge ..	43	23	20	4·9
Belfast	19	20	24	8·3

Although the incidence of old lesions appears to be much higher in Glasgow than in the other universities (Table II), the results depend so much on the method of reporting miniature films that their significance is open to question.

Table III.—(*B*) *Previously Diagnosed, Requiring Observation*

University	1950–1	1951–2	1952–3	Incidence per 1,000
Edinburgh ..	6	12	14	1·8
Glasgow	35	22	42	5·1
Cambridge ..	9	11	9	1·7
Belfast	6	5	9	2·6

Among the group showing lesions previously diagnosed, Glasgow is again a long way in the lead (Table III).

Table IV.—(*C*) *Newly Discovered Significant Lesions Requiring Immediate Treatment or Further Observation*

University	1950–1	1951–2	1952–3	Incidence per 1,000
Edinburgh ..	16	20	12	2·6
Glasgow	10	20	25	2·8
Cambridge ..	12	9	6	1·5
Belfast	11	8	7	3·4

Table IV shows the significant lesions newly discovered. Here Belfast is in the lead with 3.4 per 1,000 students.

Table V.—(*D*) *Doubtful Appearances Requiring Observation*

University	1950–1	1951–2	1952–3	Incidence per 1,000
Edinburgh ..	7	6	7	1·6
Glasgow	20	25	?	3·5
Cambridge ..	6	20	19	2·6
Belfast	6	—	1	0·9

The figures in category D (Table V) like those of A, are difficult to compare accurately, and require no further comment.

Table VI.—*Total Active Cases (that is, B plus C)*

University	1950–1	1951–2	1952–3	Incidence per 1,000 at Risk	Incidence per 1,000 Examined
Edinburgh ..	22	32	26	4·4	6·2
Glasgow ..	45	42	67	7·9	12·6
Cambridge ..	21	20	15	3·2	4·9
Belfast ..	17	13	16	6·1	6·5

Table VI shows the incidence of active tuberculosis in the four universities. These cases have been picked up not only by means of the mass radiography survey but from routine clinical examinations and, in the case of Edinburgh and Belfast, during routine treatment for incidental illness.

Results of Tuberculin Sensitivity Survey

In Table VII the result of tuberculin-testing 11,065 first-year students and nurses in 10 university centres is presented. The Belfast figures include students of all faculties, but in the other centres the figures refer to medical, dental, and veterinary students and student nurses in general hospitals—a population known to carry a greater risk of exposure to tuberculous infection than students of other faculties. The findings in men and women students have been listed in separate columns, as there is a clinical impression that women students show a lower degree of tuberculin sensitivity than men of corresponding age. This survey appears to confirm this, since between the men and women students there is almost 8% difference. This difference may partly be

Table VII.—*Tuberculin Sensitivity of Students (Men and Women) and Student Nurses at Commencement of Training (October, 1949, to June, 1954)*

University	Students				Nurses		Total	
	Men Tested	Neg. (%)	Women Tested	Neg. (%)	No. Tested	Neg. (%)	No. Tested	Neg. (%)
Aberdeen ..	209	22·0	77	32·5	462	43·5	748	36·4
Belfast ..	1,729	25·9	681	33·5	—	—	2,410	28·1
Birmingham	354	33·6	92	28·3	—	—	446	32·5
Cambridge	259	30·9	21	52·4	—	—	280	32·5
Dublin ..	509	28·7	196	43·4	—	—	705	32·8
Edinburgh	1,003	24·1	334	31·4	1,116	29·1	2,453	27·4
Glasgow ..	958	24·5	235	34·0	—	—	1,193	26·4
Leeds ..	302	23·2	70	24·3	—	—	372	23·4
Oxford* ..	—	—	—	—	600	30·2	600	30·2
Sheffield ..	465	18·7	104	20·2	1,289	21·8	1,858	20·9
Total ..	5,788	25·4	1,810	33·0	3,467	28·5	11,065	27·6

* The Radcliffe Infirmary, Oxford United Hospitals.

accounted for by the slightly older age group of the men, since a small percentage of first-year students have already completed National Service.

The 1,116 first-year nurses in Edinburgh include a group, 1,006 nurses, starting training in the Royal Infirmary: of these, 201 had completed more than 18 months' training in some other hospital. Of the untrained 32% did not react, compared with 17% of the previously trained.

Nurses recruited from the industrial area of South Yorkshire to train in the Sheffield United Hospitals show a big contrast in their degree of tuberculin sensitivity to those girls who come from the north-east area of Scotland to train at the Aberdeen Royal Infirmary.

The majority of university centres approximate the average of 27.6 negative reactors, with the exception of Aberdeen and Sheffield.

Methods of Tuberculin-Testing

Initially all centres used the Mantoux test with old tuberculin 1/10,000, 1/1,000, and 1/100.

The routine use of 1/1,000 old tuberculin as an initial screening test was found by experience to cause some unpleasantly severe reactions. It was necessary before testing, therefore, to question each student about any known contact with tuberculous infection in his family, friends, or other associates. By giving an initial dose of 1/10,000 to those suspected of exposure the number of severe reactions was greatly diminished. This method of screening is, however, time-consuming.

We are indebted to Drs. Gifford and Worth, of Sheffield University, for introducing the Heaf multiple-puncture method of tuberculin-testing (Heaf, 1951). This method has several advantages over the Mantoux test: (1) It does not produce such severe reactions, even in those highly sensitive to tuberculin, and thereby obviates screening by preliminary interrogation. (2) It is more efficient than the Mantoux method, and the positive and negative reactions are more clearly defined. (3) It can be carried out with greater speed than the Mantoux test: with fully organized team-work it is possible to test 180 students in one hour. (4) It is less painful than the Mantoux method and seems to appeal to the student mentality.

It is our practice to screen all students by means of this simple test, and the negative reactors are rechecked two days before B.C.G. vaccination with a 1/100 Mantoux test. The Heaf method has proved satisfactory as a post-vaccination test of conversion. The post-B.C.G. positive reaction is uniformly shown by six discrete areas of erythema. If superinfection by the tubercle bacillus has occurred the whole area is erythematous and indurated.

Special attention has been paid to the difference in the Mantoux reaction following natural conversion and that which is seen following B.C.G. vaccination. In the post-B.C.G. Mantoux reaction there is usually a wide area of erythema, but considerably less induration of the skin than is seen in the natural conversion. The post-B.C.G. reaction is consequently rarely painful, and has, in our experience, never caused systemic disturbances.

Significance of Severe Reactions to the Initial Tuberculin Test

When the student shows a high degree of cutaneous sensitivity and systemic disturbances following the initial tuberculin test, it is our practice to take a full-size radiograph of the chest and repeat it again in five months. We have picked up six cases of pulmonary tuberculosis, each in an early stage, by this practice (all students having been previously screened by means of mass radiography).

We have had such confidence in the efficiency of B.C.G. vaccination that when, in the course of the annual recheck tuberculin test after vaccination, there is found to be a superinfection tuberculin reaction—seen most commonly in medical students during their fourth year and at an earlier stage in student nurses—no action has hitherto been taken to investigate its significance (see below).

Tuberculin Sensitivity in Relation to Year of Training

The study of tuberculin sensitivity of medical students and nurses during the various years of training elicits some very illuminating facts concerning the infection rate, and demonstrates the danger to which these young people are subjected.

Houghton and Horne (1950), in their study of tuberculin sensitivity in medical students and nurses in Edinburgh in relation to the year of training during the year 1948–9, showed that conversion from negative to positive reactors occurred at the rate of 4–5% per annum during the medical students' clinical years, and from the commencement of training in hospital nurses. In Glasgow, prior to the use of B.C.G. vaccine, Dr. A. Stewart Henderson (personal communication) followed a class of medical students of whom 24.7% had been negative reactors in the first year and found that only 14.5% failed to react by the end of the third year of study. These observations, coupled with the fact that the maximum incidence of tuberculosis is in third- to fifth-year medical students and in second-year nurses, were cogent arguments for a measure of compulsion in relation to annual radiography. From these studies it was also clear that the most vulnerable student was the negative reactor who was exposed to infection for the first time.

Pathogenesis of Tuberculosis in Young Adults

One-quarter of the students beginning study in the medical faculty and almost one-third of young women entering the nursing profession have not been infected previously by the tubercle bacillus. In the course of training almost every student or nurse acquires tuberculous infection.

Approximately six weeks after exposure to infection the Mantoux-negative-reacting young adult converts to a positive Mantoux reaction. It is our impression that the higher the degree of sensitivity to tuberculin as shown by this reaction, the greater the danger of ultimate progressive tuberculosis (20 mm. or more of induration following 0.1 ml. of 1/10,000 old tuberculin is considered to show high sensitivity).

In Edinburgh a series of student nurses have been admitted to hospital following the phase of conversion, and have been studied in detail. They have variable symptoms of a vague nature. They have complained of the insidious onset of lassitude and undue fatigue following physical and mental effort. Rectal temperatures observed at this time show a slightly greater morning and evening fluctuation than normal. The pulse rate accelerates unduly on exercise and may be relatively rapid during periods of rest. The blood sedimentation rate may rise above the normal level. In a small percentage of cases, particularly in young women, erythema nodosum may develop (we have seen erythema nodosum only once in a male student). This phenomenon would appear to indicate a very high degree of sensitivity to the tuberculosis toxin, and we believe it is ill omen for the future. Between 1941 and 1949 eleven nurses developed erythema nodosum: three of these have recovered without subsequent evidence of clinical tuberculosis, two developed pleurisy with effusion alone, three pleurisy with effusion and a subsequent lung lesion, two a progressive pulmonary tuberculosis, and one a spinal tuberculosis.

It would appear that the inhaled tubercle bacilli may gain access to the lung at any point to form a primary focus. The careful pathological study of these lesions, carried out by Medlar (1948) in New York, showed that these foci have no particular site of election in the lung field, although the Prophit Survey showed a slight predilection for the upper zone (44%), with 25% mid-zone and 31% in the lower zone. Infection spreads from the primary focus to the hilar glands via the peribronchial lymphatics and may thence reach the blood stream through the thoracic duct.

Myers *et al.* (1937) made a detailed study concerning the pathogenesis of primary tuberculous infection in 12,000 students of the University of Minnesota, and concluded that the primary infections in young adults are innocuous and

self-limiting, and require no special treatment. These observations do not apply to students in Edinburgh, and substantiate the statement made by Pinner (1947) that "tuberculosis changes with time and place. For this reason every country, and possibly smaller subdivisions, must investigate their local epidemiological conditions; none can accept, without proof, the findings in some other regions."

Studies on the pathogenesis of primary tuberculosis of young adults in various parts of the world appear to substantiate the belief that a certain percentage—the number depending on such varying conditions as intensity of infection and native resistance—proceed to progressive tuberculosis. In this country the Prophit Survey showed that pulmonary tuberculosis occurred three times as frequently after primary infection as it did after reinfection. (The morbidity rate was 23.1 per 1,000 in young adults who were initially tuberculin-negative, compared with 7.3 in those tuberculin-positive.)

In Europe, and particularly in Scandinavian countries, Frostad (1944), Hedvall (1946), and Malmros (1947) have all pointed out that while adult primary infections are usually non-progressive and non-productive of symptoms or radiological changes, they not infrequently are progressive and malignant. Pinner (1947), in America, has also emphasized the danger of progressive tuberculosis following primary infections in this age group.

How, then, can we lessen the danger to our Mantoux-negative students? The answer must be (1) to remove, so far as is possible, all sources of infection from the community in which these young people live (the practical difficulties in putting this measure into effect in relation to medical students and nurses are obvious), and (2) to immunize them with a known quantity of tubercle bacilli of limited pathogenic properties which will allow a natural Mantoux conversion without the risk of progressive disease.

B.C.G. Vaccination of Medical Students and Nurses

In November, 1949, the first batch of 34 Mantoux-negative nurses in the Royal Infirmary of Edinburgh were vaccinated with B.C.G. vaccine. In this procedure 0.1 ml. of B.C.G. vaccine (which represents approximately 1,000,000 live tubercle bacilli of an attenuated bovine type) is injected intracutaneously into the left deltoid area. Within 10–20 days a small red nodule develops at the site of injection: it becomes a little tender, and in about 10% of cases disappears over a period of six weeks. In about 90% of vaccinations a tiny drop of purulent material exudes from the surface of the nodule, desquamation or ulceration may occur, and healing may take from six weeks to three months. In a small percentage of cases the axillary glands may enlarge and become slightly tender. If the injection is given subcutaneously an unpleasant ulcer will develop at the site and regional adenitis may supervene; so far we have not seen any case of this kind.

Students are Mantoux-tested eight weeks after vaccination, and in almost 100% of cases there is a conversion to a positive reaction. The very few who do not convert are revaccinated. Danish vaccine has been used in almost all cases; it has been found to be very constant in its reactions, and the subsequent annual Mantoux retest has remained positive in almost 100% of cases.

Table VIII shows that during the past 4½ years 2,630 students and student nurses have been vaccinated with B.C.G. vaccine in the ten university centres. No untoward reactions following vaccination have been recorded. In all, 19 students failed to convert to a positive Mantoux reaction after vaccination. This failure to convert is probably the result of faulty technique in injecting the vaccine, and a second injection is almost invariably successful. There are three students, however, reported from Sheffield, Glasgow, and Edinburgh, who have remained negative reactors even after repeated vaccination with vaccine of proved potency. The cause for this phenomenon remains a mystery.

Forty-one students are recorded as having reverted to negative at the subsequent annual testing. The large number reported from Edinburgh is accounted for by the fact that a batch of 92 students were given B.C.G. vaccine from the Pasteur Institute, Paris. Despite the fact that double the recommended dose was administered 30% have required revaccination with Danish vaccine.

It is with a sense of disappointment and regret that two cases of pulmonary tuberculosis are reported in vaccinated students, and one in a vaccinated nurse.

(1) A Mantoux-negative male student of University College, Dublin, was given B.C.G. vaccine in November, 1951, and in June, 1952, was found to have active, non-cavitated, unilateral infiltration. This case is reported by Dr. Michael Moriarty.

(2) A male student from Yorkshire began the study of medicine in Edinburgh in October, 1949. He was Mantoux-negative (1/100) in December, 1949. He was vaccinated with Danish vaccine on December 12. A large film of the chest on December 12 was negative, but a note was made that there was a ? calcified shadow in the left hilum. He was retested in February, 1950, and in each subsequent year, giving 10, 8, and 5 mm. of induration in successive tests. In February, 1954—that is, during his fifth year of study—he gave a florid positive reaction which was noted as a superinfection reaction. On May 12, 1954, he developed acute tonsillitis and three days later had a small haemoptysis. Chest *x*-ray examination showed faint patchy opacities in the left upper and mid-zones, suggestive of early tuberculous infiltration. *X*-ray sinuses showed left maxillary sinusitis. The B.S.R. was 9 mm. per hour. He was treated with intensive penicillin therapy, but on June 6 chest *x*-ray examination showed the opacities in the lung to be more definite. Culture from gastric lavage has grown tubercle bacilli. He was given chemotherapy and has since had a segmental resection.

(3) A Royal Infirmary of Edinburgh nurse, aged 18, began training on January 1, 1950. She was first tuberculin-tested on January 15 and was found to be negative to 1/100 old tuberculin. On February 3 she was vaccinated with B.C.G. (Pasteur) and a small papule 4 mm. in diameter was observed on April 2, when an induration of 12 mm. to 1/1,000 O.T. was observed. Subsequent testing on November 4, 1950, and November 27, 1951, showed induration of 5 mm. to 1/1,000 O.T. On December 13, 1952, the induration was recorded as 20 mm., suggesting that she had been reinfected. Appendicectomy was carried out in December, 1953, and in April, 1954, she began to feel tired, had a cough, with production of greenish sputum, and complained of pain in the left side of chest. An *x*-ray film showed extensive tuberculous infiltration in the left apical segment and also in the right intraclavicular area. The B.S.R. was 43 mm. per hour. Sputum contained numerous tubercle bacilli. She has begun chemotherapy.

TABLE VIII.—*B.C.G. Vaccination of Students and Student Nurses, November, 1949, to June, 1954*

University	No. Vaccinated	No. of Untoward Reactions	No. Failing to Convert	No. of Reversions to Negative	No. since Showing Evidence of Tuberculosis
Aberdeen ..	272	0	0	1	0
Belfast ..	490	0	3	3	0
Birmingham ..	133	0	3	0	0
Cambridge ..	57	0	0	0	0
Dublin ..	188	0	5	0	1
Edinburgh ..	785	0	3	30	2
Glasgow ..	279	0	0	3	0
Leeds ..	87	0	3	0	0
Oxford ..	4*	0	0	0	0
Sheffield ..	335	0	2	4	0
Total ..	2,630	0	19	41	3

* 146 were vaccinated with vole vaccine: 100% successful protection so far.

Control Observations

If this investigation had been planned and carried out as a research project alone, half the Mantoux-negative reactors would have been left unvaccinated; however, we could not withhold the vaccine from those who requested protection by this method.

Table IX shows that 392 students or nurses, initially tuberculin-negative, had not received B.C.G. vaccine. Of these 14 have developed clinical evidence of tuberculous infection. Thus, six are reported from Queen's University, Belfast; one male Glasgow medical student developed in

TABLE IX.—*Negative Reactors not Vaccinated*

University	Not Vaccinated	Subsequent Evidence of Tuberculosis
Aberdeen	10	0
Belfast	176	6
Birmingham ..	12	0
Cambridge ..	34	0
Dublin	38	0
Edinburgh ..	31	7
Glasgow	36	1
Leeds	0	0
Oxford	1	0
Sheffield	54	0
Total ..	392	14

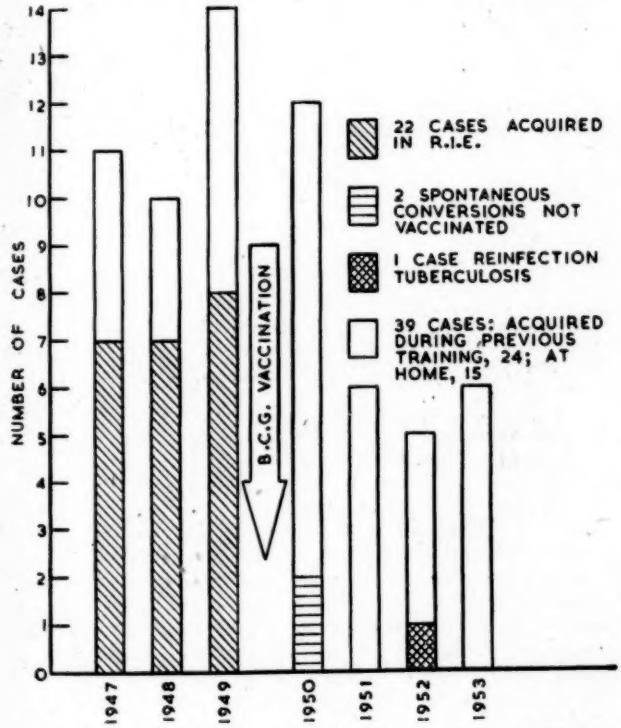
his third year tuberculous pleurisy with effusion; and in Edinburgh seven have developed tuberculous lesions—that is, pleurisy with effusion (4), tuberculous mediastinal adenitis (1), progressive apical infiltration (1), and non-progressive primary focus in the right lower lobe (1). This incidence of 22% is strikingly higher than in other centres.

Result of Prophylactic Measures

In vaccinated students there has been an incidence of tuberculosis of 0.11%, whereas in controls the incidence is 3.32%. These results are remarkably similar to those published by Wells and Wylie (1954).

Incidence of Tuberculosis in the Nursing Staff of the Royal Infirmary of Edinburgh, September, 1946, to September, 1953

During the past seven years there were 64 cases of tuberculosis in nurses on the staff of the Royal Infirmary (which includes the Simpson Maternity Pavilion). The accompanying Chart shows that this total is made up of the following groups. There were 22 cases (7, 7, and 8 in the years 1947, 1948, and 1949 respectively) in which the infection was acquired in the course of training; these represent examples of erythema nodosum, pleurisy with effusion, and primary lesions of the lung parenchyma. The two cases in 1950 occurred after spontaneous conversion to a positive tuberculin reaction prior to the administration of B.C.G. vaccine; these cases have already been referred to: one developed



Incidence of tuberculosis in nurses of the Royal Infirmary, Edinburgh, 1947–53.

evidence of mediastinal adenitis and the other pleurisy with effusion. In 1952 one case occurred which appeared to be an example of reinfection tuberculosis. This nurse from Sutherland was Mantoux-positive when she began her training; in her fourth year she developed a caseating tuberculous gland in her neck and subsequently infiltrating lesions in the apices of both lungs. Thirty-nine nurses were found to have active or chronic tuberculous lesions which had been acquired before joining the staff of the hospital; of these, it seemed probable that 24 had acquired infection in the course of training at a previous hospital and 15 had been infected either at home or at school.

It is very gratifying to note that from November, 1949, since when all Mantoux-negative-reacting nurses have been vaccinated with B.C.G. vaccine, only one initially tuberculin-negative nurse has contracted tuberculosis. This fact appears to be very strong testimony in favour of prophylactic vaccination.

Conclusion

When we look at a chest film of a student showing a tuberculous lesion, we should always be aware of its wider implications—the time lost, the expense, the altered life plans, the frustrated ambitions, the deterioration of general physical status and emotional stability, and the ultimate and ever-present fear of possible relapse: such a tragedy has befallen approximately seven in every thousand of our students. This is therefore no mean problem.

Summary

The average incidence of pulmonary tuberculosis in students of the Universities of Edinburgh, Glasgow, Cambridge, and Belfast over a three-year period was 2.6, 2.8, 1.5, and 3.4 per 1,000 respectively.

Tuberculin sensitivity tests on 11,065 first-year students and nurses in ten university centres show an average of 27.6% negative reactors—Aberdeen having the highest, 36.4%, and Sheffield the lowest, 20.9%.

The advantages of the Heaf test over the Mantoux test as a method of screening are stated.

The ominous significance of extreme skin sensitivity to tuberculin, of the superinfection tuberculin-reaction, and of erythema nodosum in young adults is demonstrated.

The pathogenesis of pulmonary tuberculosis in young adults is outlined, showing the danger of the primary infection at this stage of life, and the need for protection from infection and for prophylactic vaccination.

Among 2,630 tuberculin-negative students and nurses vaccinated with B.C.G. vaccine there were no untoward reactions; 0.72% failed to convert after the first vaccination; 0.11% remained negative reactors after repeated vaccinations; 1.44% reverted to negative within 1–5 years; and 0.11% ultimately developed pulmonary tuberculosis.

Of the control group of 392 non-vaccinated negative reactors, 3.32% developed clinical evidence of tuberculous infection.

The incidence of tuberculosis in the nursing staff of the Royal Infirmary of Edinburgh for a seven-year period in which B.C.G. vaccination was instituted is reported.

I am indebted to the following student health officers who have carried out the work which is the foundation of this paper: Dr. A. H. Macklin, University of Aberdeen; Dr. Wilson Johnson, Queen's University, Belfast; Dr. R. Bolton, University of Birmingham; Sir Alan Rook, University of Cambridge; Dr. M. A. Moriarty, University College, Dublin; Dr. Norman Horne, University of Edinburgh; Dr. Stewart Henderson, University of Glasgow; Dr. Ronald Still, University of Leeds; Dr. Clement Wells, Oxford United Hospitals; Dr. P. Gifford, University of

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THE SYMPTOMS OF HIATUS HERNIA

BY

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The symptoms of hiatus hernia are very varied and are often mistaken for those of other diseases. This led Harrington (1948) to refer to the condition as the "masquerader of the abdomen." The object of the present study is to analyse the symptoms in a series of patients with hiatus hernia. Particular attention has been paid to the occurrence of pain resembling that of cardiac ischaemia.

Material

Between May, 1952, and October, 1954, at the Bristol Royal Infirmary, barium-meal examination (with the Trendelenburg manœuvre) revealed a hiatus hernia in 70 patients, all of whom were re-examined. Sixteen of them also had another disease which could have caused their symptoms, and have therefore been excluded from this survey. The remaining 54 patients form the first group studied in this investigation.

The second group studied were seven private patients seen by Dr. D. H. Davies. They were originally sent to him because their symptoms had been attributed to heart disease. Hiatus hernia was the only abnormality found.

First Series

The series comprised 21 men and 33 women, whose ages ranged from 21 to 86 years. Forty patients were over 50 (Fig. 1). Forty-six of the patients had sliding herniae; six had paraoesophageal or rolling herniae, and two had paraoesophageal herniae with evidence of regurgitation into the oesophagus.

Symptoms (Fig. 2)

Pain was present in 32 cases (59%). In 28 it was situated in the epigastrium, and in two of these it radiated under the left costal margin. The remaining four felt it only in the left side between the left costal margin, left loin, and left scapula. It was nearly always nagging, gnawing, or described as a bloated feeling; its distribution was usually diffuse, but in several patients it was sharper, and was localized just beneath the xiphisternum. It bore no relation to meals in 17; in the remainder it occurred from a few minutes to two hours after meals, and in these patients fatty food was almost always an aggravating factor. Even where no other relation to food existed several patients said that the taking of fried food at the evening meal often caused distress during the night. The pain was relieved by antacids in nine. Three patients complained of pain when lying on the left side at night relieved by turning on the right, and in one the reverse held true. Five had pain only in the evening when fatigued, and this was not thought to be due to the postural effect of sitting back in an easy chair.

Heartburn, a burning feeling starting in the epigastrium and spreading up through the chest sometimes as far as the throat, was a complaint of 40 patients (74%). It frequently preceded other symptoms by many years. In 12 patients it followed eating, in 15 no relationship to food existed, and 23 of the 40 patients stated that it woke them from sleep. Six of the women dated the onset of their trouble to heartburn in pregnancy. When severe, heartburn was associated with acid regurgitation into the mouth, but in 10 patients this never happened.

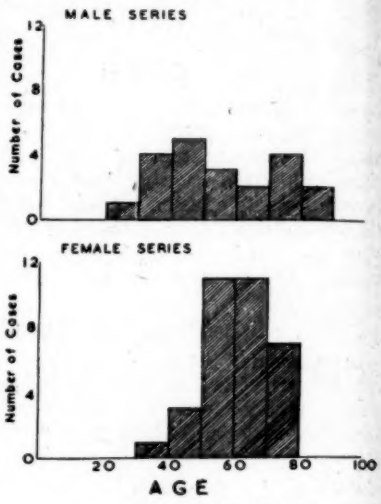

FIG. 1.—Age incidence.

Acid regurgitation was a prominent symptom in 36 patients (67%), in six of whom there was no preceding heartburn.

Waterbrash, the sudden outpouring of mouthfuls of tasteless fluid, occurred in 13 (24%). Most commonly it preceded vomiting, but it sometimes followed heartburn. Two patients were woken by waterbrash at night.

Flatulence, usually postprandial, was a complaint of 38 patients (70%).

Vomiting was present in 31 of the series (57%). In 20 it followed eating; one complained of bouts of vomiting at any time of the day, while another vomited without warning during the course of a meal. One patient had had to give up gardening as he was liable to vomit on bending forwards, and the remaining eight suffered from bouts of nocturnal vomiting, often of fairly large quantities. In most of the eight this was their presenting and most distressing symptom, and often there was no warning nausea. Three patients woke with nausea if they lay on the right side, but sitting up or turning on the left side relieved it and vomiting did not occur.

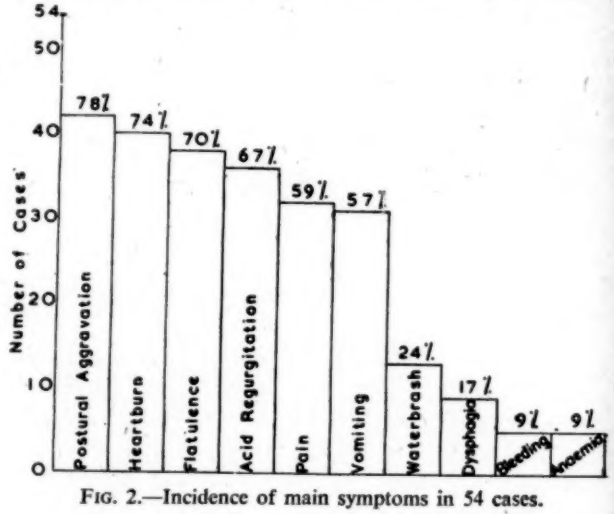

FIG. 2.—Incidence of main symptoms in 54 cases.

Symptoms were aggravated both on lying down and on bending forward, as to fasten a shoe in 24, while 10 could

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bend forward with impunity, distress being caused only on lying flat. In the remaining 8 the reverse was true. Symptoms thus provoked varied from patient to patient, but were usually heartburn (with or without acid regurgitation), vomiting, occasionally acid regurgitation alone, epigastric pain, or waterbrash. This relationship to posture was well marked in 42 (78%).

Dysphagia was present in nine patients (17%), in eight of whom food tended to stick momentarily behind the lower sternum before passing on; in two the sensation was accompanied by a feeling of slight burning in the throat. The remaining patient said that food burned all the way down but there was no actual difficulty in swallowing.

Appetite was almost always described as good or very good. Eighteen patients were gaining weight, a few were losing, often deliberately, and in the remainder the weight was constant. Sixteen of the men and 18 of the women were obese.

Palpitations and effort breathlessness were complaints of a few of the elderly obese patients, and were not attributed to the herniae.

Exertion itself never aggravated a patient's symptoms except when in the stooping position, as in gardening, where posture played a part.

Five patients (9%) gave a history of internal haemorrhage (melaena in three, haematemesis in two), and three others had intermittently blood-streaked mucus. Another five (9%) (two men, three women) had histories of anaemia, sometimes recurrent, which had responded to iron and for which there was no clear cause.

Relation to Trauma

Two patients gave a history of sudden onset following trauma.

Case 8.—A man of 44 had heartburn during the war years, aggravated by stooping. It was never severe, however, and had been absent for 10 years. One day a ladder was falling on him; he caught it with his arms over his head and broke its fall. Immediately he had a severe pain over the upper abdomen and lower chest which lasted several hours. He rested and by next day felt better. One month later the pain returned over the same site, but not so severely. It occurred most days and bore no relation to food, but was aggravated by lying down. A hiatus hernia was found on *x*-ray examination. Medical treatment did not relieve his symptoms, which disappeared after repair of the hernia a year later.

Case 34.—An obese woman of 55 described the onset in these words: "On Monday, May 9, 1952, at 11 a.m., I was stooping forward, lifting a bed, and I lifted my right foot to kick the carpet away, when I got the most intense gripping pain in the middle of my abdomen, spreading up to the lower part of my chest. I dropped the bed and fell to the floor, almost fainting. I wanted to vomit, so I crawled along to the lavatory, where I vomited all I had. I lay down for two hours, but the pain was not better and I was taken home by car. It got worse and worse, and I kept vomiting, and the following day was taken to the local hospital, where I lay for three days, getting no better. They were very worried about me and did not know what was the matter. On the Friday morning, four days after lifting the bed, I felt I wanted to stretch myself up for miles, and I gripped the overhanging pulley and pulled myself up. As I did so I felt as if something was dropping downwards from the upper abdomen, and it gurgled. Immediately I was relieved and the pain left the upper part of my stomach. I did it again a few minutes later, and it went completely and I was better. The vomiting stopped and I never looked back, but the upper part of my stomach was sore to the touch for months. I do not bend down any more, as I get the pain again, though of course nothing like so bad, and I sleep propped up, as I get it if I lie flat." She stoutly denied any trouble before May 9, 1952. *X*-ray examination showed a hiatus hernia.

Second Series

Since chest pain which might be confused with that of myocardial ischaemia was not a feature of any patient in the first series, a further group of seven patients with pain attributed to heart disease were studied. They had been referred privately to a cardiologist, but were subsequently shown to have a hiatus hernia.

Summaries of Histories

Case 1.—A woman of 63 was subject to heartburn and acid regurgitation, epigastric pain, and flatulence when lying on the right side at night. She also complained of wind behind the sternum spreading up into the neck and lower jaw and rarely to the left arm, which occurred on exertion and sometimes stopped her if she was walking quickly. It was relieved as soon as she had brought the wind up, and she said that it was "the wind that stopped me, not the pain." The symptoms varied greatly from day to day. A barium-meal examination showed a fairly large hiatus hernia; physical examination, heart screening, and the electrocardiogram were all normal.

Case 2.—A man of 48 had suffered from bouts of severe flatulence lasting several weeks every year since his early twenties. They were worse at night, and he was often woken at 2 a.m. with wind in the upper abdomen and "under the heart," which was always relieved by belching. Recently pain had spread to the left arm and, very rarely, to both arms, though this had occurred only in the daytime. The symptoms were never related to exertion, but were always aggravated by fatigue or worry. No evidence of organic heart disease was found. A hiatus hernia was revealed on barium-meal examination.

Case 3.—A woman of 70 who suffered from acid regurgitation at night had recently had attacks of pain in both wrists, spreading up the arms and across the shoulders. They occurred at any time of the day, though never at night, and bore no relation to exertion. A month before being seen she had had a choking feeling in the chest lasting 15 minutes. This had never recurred. Physical examination, electrocardiogram, and heart screening were normal. Hiatus hernia was found on barium-meal examination.

Case 4.—A woman of 68 complained of occasional heartburn when in bed, and heartburn and acid regurgitation on bending forwards after a meal. Three months previously, when out walking, she experienced pain in the mid-chest, which spread through to the back and into the left arm and forced her to stop momentarily with relief. She had never had it again, and felt now that she could walk a long way without any trouble. Two weeks before being seen a similar pain had woken her at night on several occasions and lasted about 10 minutes. It was relieved by sitting up. She had been given nitroglycerin tablets, and felt that they might have helped her a little. No abnormal signs were present on examination, and screening and electrocardiography were normal. A small hiatus hernia was shown on barium-meal examination.

Case 5.—A man of 67 complained of intermittent hot burning pain behind the mid-sternum of four years' duration. It occurred in bouts of a week's duration, the pain coming after eating and being aggravated by further swallowing: it always spread through to the back. Recently an attack of similar pain had woken him during the night. There was no relation to exertion. Physical examination revealed no abnormality. An electrocardiogram showed right bundle-branch block. Barium-meal examination revealed a small hiatus hernia.

Case 6.—A man of 58 was first seen in 1949, when he complained of slight effort breathlessness with occasional epigastric pain on effort; this also occurred half to three hours after food and was relieved by belching. About this time he had one severe attack of abdominal pain at night lasting several hours, and following this an investiga-

tion revealed a hiatus hernia. An ulcer diet relieved all his symptoms until 1952, when he again had two bouts of very severe abdominal pain in the xiphisternal region at night. No clinical, electrocardiographic, or radiological evidence of heart disease was found, and he had no further trouble after repair of the hernia.

Case 7.—A woman of 72 was referred with paroxysmal auricular fibrillation. She gave a history of typical cardiac effort pain 30 years previously due to anaemia associated with hiatus hernia. The anaemia had responded to iron treatment. She had had no pain since. Physical examination revealed signs at the left base thought to be due to a hiatus hernia; a barium-meal examination confirmed this, a large hernia being present behind the heart.

Discussion

Two main types of hiatus hernia are recognized in adults —the sliding and the rolling—and their symptoms are considered to be different. In the sliding type the whole of the lower end of the oesophagus and upper portion of the stomach are periodically or permanently in the chest. In this type the symptoms are mainly those attributed to regurgitation of gastric contents into the lower oesophagus; thus there is heartburn and regurgitation of acid into the mouth, commonly occurring on bending forward or lying down. Flatulence is common and dysphagia varies from slight discomfort to severe pain. The pain may radiate from the upper abdomen and lower chest to the neck, jaw, palate, and into the left arm, or occasionally both arms. Symptoms attributed to the presence of a portion of the stomach within the chest are uncommon in the sliding hernia. In the second type, the rolling or paraoesophageal hernia, the fundus of the stomach rolls up in front of the oesophagus through the oesophageal hiatus. The cardia usually remains below the diaphragm and regurgitation is said to be uncommon. The symptoms of oesophagitis are therefore rarer, and flatulence, upper abdominal pain, and attacks of vomiting for several days with remissions of several weeks mainly occur.

As only six paraoesophageal herniae without radiological evidence of regurgitation were present in the series of 54 cases no conclusions regarding their special symptoms can be drawn. It is interesting, however, that in two of the four instances where only left-sided pain extending to the left scapular region occurred a rolling hernia was found. Apart from this no difference in the symptoms of the two types was noted.

Allison (1951) gave an excellent composite account of hiatus hernia complicated by oesophagitis, stressing the frequency of the latter in hiatus hernia. As oesophagoscopy was carried out in few of the present series the actual incidence of oesophagitis is unknown. However, although heartburn and acid regurgitation were common, only one of the 54 patients complained of burning pain on swallowing. Bouts of vomiting, usually nocturnal, and frequently unaccompanied by nausea or other symptoms, occurred in eight patients. All had sliding herniae.

Most observers agree that hiatus hernia occurs more often in women, though Harrington found it to be commoner in men. In the present series women outnumbered men in the ratio of 3:2. The increasing incidence in the female sex with age (Belsey, 1952) is shown in the present series, 10 of the 21 men being under 50 years old, as compared with only 4 of the 33 women. The relation to obesity is well known, and 34 of the first series were overweight. However, this made little difference to the severity of their symptoms. The two instances when trauma played a part are interesting in that both episodes seemed to bear a direct relation to the onset or recurrence of symptoms. Traumatic diaphragmatic hernia due to indirect violence is well known (Harrington, 1948) and results normally from external violence, the most common cause being road accidents. More often than not it is left-sided, with the defect in the diaphragm situated in the apex or posteriorly. On rare occasions, however, it may extend up through the normal oesophageal hiatus (Chamberlain and Ford, 1953); this appears to have occurred in the present cases.

Relation to Angina Pectoris

Reid (1940) described a patient, a doctor, who suffered from recurrent bouts of severe pain in the chest and left arm which lasted for between a few minutes and five hours. The pain bore no direct relation to exertion, tending to occur with anxiety or swallowing hot food, and at night. Though physical examination and electrocardiography showed nothing abnormal it was thought for many months that myocardial ischaemia was the cause of the symptoms. A barium-meal examination then revealed a hiatus hernia, medical management of which relieved the trouble. Jones (1941) was impressed by how often the clinical histories of his patients with hiatus hernia suggested organic heart disease; he stressed, however, that "in no case did exertion invariably produce pain" and "in no case was the relief of symptoms following the use of nitroglycerin as regular as that noted in typical anginal attacks."

Wyburn-Mason (1948), in illustrating instances of anginal pain and the normal heart, quotes an example of a woman of 57 who for two years had suffered intermittently from epigastric and substernal pain radiating to the interscapular region and both arms, especially the left. She also had numbness and tingling in the fingers of the left hand independently of the "anginal" attacks. The pain occurred a quarter of an hour after meals, was sometimes accompanied by vomiting, was often of considerable severity, and made her afraid to eat. It bore no relation to exertion. A hiatus hernia was the only clinical finding. Master *et al.* (1949), from a study of 57 patients with hiatus hernia using the anoxaemia test, found six patients in whom thoracic pain was suggestive of angina pectoris. They suggested that the history was not a safe method of distinguishing the pain from that of coronary disease, but admitted that it was helpful, taking into account postural effects, relation to exercise, and drugs. Baylis *et al.* (1955) concluded from a study of oesophageal distension that pain as produced by experimental distension of the lower third of the oesophagus differed from that of cardiac ischaemia in its character, its fluctuating nature, the speed of its precipitation and abolition, and the absence of electrocardiographic change. They felt, however, that electrocardiography offered the most reliable means of distinguishing between the oesophageal and cardiac pain.

Nuzum (1952) found hiatus herniae in 25 of 100 private patients with angina pectoris, and on review considered that 7 of the 25 did not in fact have organic heart disease and that the hernia was responsible for the pain. In one the chest pain was relieved when the haemoglobin was raised from 46% to 90%, and was probably true cardiac pain, the electrocardiogram being abnormal; but in the remaining six patients pain was present in the epigastrium and lower sternum, sometimes radiating into the shoulders and arms or neck, and often bore a relation to meals. It frequently occurred on, or was aggravated by, lying down, and was relieved by sitting up. It sometimes lasted for hours or days. One patient, followed up for 14 years, had vague epigastric pain spreading up to the chest after taking food. Ten years after the onset the nature of the pain changed to that typical of myocardial ischaemia, and the electrocardiogram became abnormal. Four years later she died from a myocardial infarction. Donnelly (1953) described the case of a male clerk aged 39, with central clenching chest pain on exertion relieved by standing still for a moment. It was worse on bending forward, and slight discomfort in the chest was present for a few moments almost immediately after getting into bed. The electrocardiogram was normal, as were two barium-meal examinations; using abdominal compression of up to 60 mm. Hg, however, a hernia was shown at the third barium-meal examination. The symptoms in this patient are very suggestive of myocardial ischaemia.

In the present investigation, though many of the patients were elderly, none of the 70 from whom the first series is taken had pain which could be confused with that of myocardial ischaemia. The seven patients in the second series were referred privately to a cardiologist, as their symptoms were thought to be due to heart disease. In Case 1 pain and "wind in the chest" on walking, and relieved by stopping to belch, was suggestive of cardiac effort pain. However, the exertion necessary to provoke an attack varied considerably from day to day. This with the history of dyspepsia and the normal cardiological finding led to the correct diagnosis. Pain in the chest (Case 5), in the chest and left arm (Case 4), and at the xiphisternum (Case 6) could have been mistaken for the pain of myocardial ischaemia, had the patient been seen in the first attack only. Again, diagnosis was assisted by the variation of the attacks over a period of time, the dyspeptic symptoms, and absence of significant cardiac disease. In Case 7 a history of genuine cardiac effort pain was related to anaemia and disappeared following iron treatment. No confusion arose in Cases 2 and 3.

It would appear, therefore, from the present study and from the literature reviewed here that hiatus hernia (in the absence of associated anaemia) may only rarely be responsible for pain in, or spreading to, the chest, arms, neck, and jaw. When this does occur it may have the same distribution as the pain of cardiac ischaemia, and the type of pain may be similar. Direct relationship to exertion, however, is very inconstant, and when present the effort required to produce the pain varies much more than in myocardial disease. Furthermore, it often lasts for hours. The predominant aggravating factors are the taking of food, the horizontal position, and, as most authors stress, anxiety. Its relief with belladonna and antacids is usually better than with nitroglycerin.

Summary and Conclusions

In 54 of 70 consecutive cases in which a hiatus hernia was found this was the only detectable lesion. The symptoms in this group were epigastric pain, heartburn, acid regurgitation, flatulence, vomiting, and waterbrash. Postural aggravation frequently occurred. The relation to trauma in two patients is described and the presentation of eight patients with attacks of vomiting is stressed. In none of these 70 patients did pain occur which could be confused with that of myocardial ischaemia.

A further seven patients referred with cardiac symptoms are analysed and the occurrence of pain in hiatus hernia simulating that of myocardial ischaemia is discussed with special reference to the literature. It is concluded that this is a very rare feature of hiatus hernia.

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TREATMENT OF HEART FAILURE*

BY

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It is natural to expect that advances in treatment should follow a better understanding of the mechanism and dynamics of heart failure, and during the past decade there have been notable advances in practically all branches of medicine. A year or so ago I listened to a physician returning thanks for a presentation on his retirement, and the theme of his valedictory speech was that he was sorry to go because he felt that the Golden Age of medical treatment was just beginning, but that perhaps it was as well, for a knowledge of Latin and Greek no longer helped him to keep pace with the bewildering names of new drugs; and, if he bothered to open his morning mail, there was apparently one new preparation a day, although some differed only very slightly from drugs he was already using.

In the treatment of heart failure, however, digitalis, introduced in 1785 by William Withering of Stafford, a great physician and medical botanist, still reigns supreme, and Wenckeback's statement made in 1910 needs no modification to-day. "Digitalis therapy," he remarked, "is one of the most important and serious duties of the general physician. It demands a great deal of skill, power of observation, keen interest, and experience. A long life is too short to learn enough about this wonderful drug." The mode of action of digitalis was one of the first problems to be tackled by the new technique of measuring the output of the heart by cardiac catheterization, and one long controversy has now been settled. It has been proved that digitalis does indeed increase the efficiency of the failing ventricle, a view long held by the older clinicians and pharmacologists. This particular action is more impressive in left ventricular failure than in right heart failure caused by mitral stenosis, for in mitral stenosis the haemodynamic circumstances are complex and variable and not yet completely understood (McMichael, 1952).

There also remain many other problems to be solved in relation to digitalis action. Nevertheless, while mindful of Wenckeback's advice, digitalis should be given in all cases of heart failure and continued thereafter for the life of the patient when there is auricular fibrillation. Digitalis also has a place in the treatment of heart failure with normal rhythm, and there is a gathering opinion that it should be given and continued indefinitely whether the pulse is fast or slow. Some patients respond best to the folia tablets, which may have a cumulative action, some to digoxin, which is excreted more rapidly and is more expensive, and a few patients who prefer a bottle of medicine continue to take the tincture, which may lose its potency. A careful watch should be kept for signs of overdosage or individual refractoriness or idiosyncrasy. In short, digitalis therapy to date remains an art rather than a science.

A new drug, procainamide ("pronestyl"), has recently been introduced for the treatment of the cardiac arrhythmias or an attack of paroxysmal tachycardia which may precipitate heart failure. It has a quinidine-like action, depressing the heart, and it does not work

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through the vagus. After a test of 250 mg., 1 g. can be given by mouth every three to four hours, making a total of 6 g. a day until the irregularity is abolished, when it should be tailed off. It is most valuable in the ventricular tachycardias, and also works in a high percentage of the supraventricular tachycardias and occasionally in paroxysmal auricular fibrillation. Unfortunately it is unlikely to be successful in prophylaxis (Lucas and Short, 1952), and quinidine sulphate still holds its place as a valuable drug to diminish the frequency of the attacks, or even to abolish them. Procainamide, however, is a valuable addition to the pharmacopoeia and deserves a trial in heart failure resulting from a prolonged attack of paroxysmal tachycardia. If it fails we rely once again on digitalis.

Mercurial Diuretics

Although the primary defect in heart failure is impaired cardiac function, the ultimate result is disturbed renal function with salt and water retention. It is the water retention that accounts for many of the subjective and objective features of congestive heart failure, and oedema of the lungs contributes to the respiratory difficulty and puts further strain on the heart. The use of mercurial diuretics (first introduced for the treatment of syphilis) as a means of getting rid of oedema in heart failure is the greatest advance since digitalis and has provided the practitioner with many of his moments of triumph. The relief of a swollen uncomfortable patient by a few injections of, say, mersalyl or "unephral," is very satisfactory, but the search goes on for an oral preparation and one free from the dangers of mercurialism. It is well known that mercury can cause a toxic nephrosis, and, if renal excretion is impaired, symptoms of mercury poisoning such as diarrhoea, vomiting, and gingivitis may occur. So far, my personal experience of oral mercurial diuretics has been limited to chlormerodrin ("mercloran"), and I still prefer parenteral therapy in grossly oedematous patients. However, the oral preparations are useful in maintaining a patient in a relatively dry state, and they have obvious advantages for children and others who dislike injections.

Restriction of sodium as a means of treating oedema is perhaps carried out more rigorously in the U.S.A. than in England. To ensure success, the daily intake of sodium should not exceed 500 mg., and unless considerable care is taken in planning the diet and the services of a dietitian are available the result may be so unappetizing that a sick patient cannot eat it. In addition, painstaking adherence to low-sodium diets may result in vitamin deficiencies as well as inadequate general nutrition unless a wide range of low-sodium foods are available and vitamin supplements prescribed (Nutritional Implications of Sodium Restriction, 1952). I do not subscribe to the view that fluid restriction is unimportant when the sodium intake is limited, and the total fluids should not exceed 2 pints (1 litre) or so a day.

A word of warning regarding the combination of mercurial diuretics with a too severe restriction of salt intake has been given by Black and Litchfield (1951). They reported eight cases, including five fatalities, in which uraemia developed during the treatment of congestive cardiac failure with a low-sodium diet of 0.2 g. a day combined with frequent injections of a mercurial diuretic. They thought that this complication was the result of salt depletion rather than mercurial damage to the kidney, and recommended that patients placed on a diet very low in sodium and also receiving injections of mercurial diuretics for heart failure should have frequent blood urea estimations.

Cation-exchange resins are sometimes an effective adjuvant to a low-salt diet in the treatment of oedema of cardiac failure. The early hope that the use of ion-exchange resins would allow a more liberal diet and an increased salt intake has not been realized (Greenman *et al.*, 1953), and many patients would rather restrict salt than take the resins, despite the makers' assertions that preparations are now available in a palatable form. A large bulk must be ingested, the cost is high, and close chemical control is necessary during treatment. For these reasons the use of resins is usually restricted to cases of persistent cardiac failure when pitting oedema remains after two to three weeks' treatment by standard means, or when mercurial diuretics are contraindicated because of sensitivity, toxicity, or failure to respond, or during convalescence from heart failure to prevent the recurrence of oedema (Spencer and Lloyd-Thomas, 1954).

New Treatments

The latest diuretic on the market—namely, "diamox"—is the result of a new approach to the problem of salt retention and resultant oedema, suggested by the observation of Mann and Keilin (1940) that suphanilamide is a specific inhibitor of the enzyme carbonic anhydrase. This enzyme is present in many tissues, and if its action can be inhibited in the renal tubules, by causing a deficiency of hydrogen ions, an alkaline urine rich in sodium bicarbonate and potassium will result. Sulphanilamide proved too toxic and not powerful enough as a carbonic anhydrase inhibitor, but a related compound, acetazoleamide has been discovered and marketed under the name diamox. A dose of 250 or 500 mg. by mouth will certainly produce a prompt diuresis in cardiac oedema, but its action is based on ionic exchange, and it remains to be seen whether the body will learn to accommodate itself to the continued use of diamox in other ways than by the desired one of excreting alkalis and water. My guess would be that diamox is unlikely to supersede the mercurial diuretics, but it will be useful on occasions in much the same way as resins have a place in the treatment of cardiac oedema. I would emphasize, however, that it is early days to judge any drug introduced as recently as diamox.

Those of us who were in Stockholm last year for the International Congress of Internal Medicine can testify to the excellence of the Swedish Pilsener beer, and it was therefore with special interest that I read a paper by Wallgren (1954) on the use of beer as a diuretic in heart failure. It is, of course, well known that beer is a diuretic, but in some countries there is a tradition that alcohol is unwholesome for cardiac cases. Dr. Wallgren has carried out some interesting studies with measured fluid and electrolyte intakes in 20 patients suffering from heart failure caused by valvular disease or hypertension and shown that the substitution of two bottles of Pilsener beer for an equivalent amount of water in a total daily fluid intake of 1.5 litres may have positive therapeutic value, since it has a slight diuretic effect and relieves the monotony of the saltless diet. The appetite is improved, and I can think of many patients who will welcome this news.

A Medical Emergency

The treatment of left heart failure resulting in cardiac asthma is a medical emergency justifying the night-call, and few emergency treatments in adult medicine are so immediately rewarding. Morphine should be administered without delay in order to calm the patient and also reduce the sensitivity of the cough reflex and so break the vicious circle of pulmonary engorgement, made worse by dyspnoea and coughing. For a patient of average weight, ¼ gr. (30 mg.) of morphine sulphate is required, and it is best to give half of this dose intravenously and the other half subcutaneously. It is unnecessary to give atropine, which induces dryness of the mouth and is of no value in drying up the lungs, since the oedema is not the result of excessive bronchial secretion.

An intravenous injection of 0.25–0.5 g. of aminophylline is given next, and, if it is known that the patient has not taken any digitalis for the past month and there is no reason to suppose that the attack of cardiac asthma is due to myocardial infarction, digoxin, 0.5–1 mg., may be injected slowly at the same time. This is one of the occasions, however, when the administration of a large dose of digitalis occasionally results in a fatality, and perhaps it is better employed later on to consolidate improvement won by other

means. The application of venous tourniquets round the thighs for a period of one hour helps the overloaded heart by lowering the venous pressure, and the ancient art of venesection should not be forgotten. This last measure, effective alike in left ventricular failure or congestive heart failure, has rather fallen out of favour; it takes a certain amount of time and may be messy, but the result is most gratifying, and it would be a backward step if venesection fell into abeyance.

Oxygen is of value in the treatment of heart failure and especially in heart failure caused by chronic respiratory disease or cor pulmonale. In England, our climate, the coal-mines, and the industrial cities are responsible for many cases of chronic respiratory disease, but the outlook is better, for much research is going on concerning the development of pneumoconiosis and the use of smokeless fuel. Meantime, methods of giving oxygen have improved, and we frequently see oxygen cylinders leaving the store in hospital for the treatment of patients in the home. Indeed, this has become so popular that the arrival of a cylinder of oxygen or an oxygen tent is no longer regarded by the patient's relatives as a tactful reminder that they should look out the name of an undertaker.

May I make a brief reference to thyrotoxicosis, which is often overlooked as a cause of heart failure. When I was a house-physician we talked about "masked hyperthyroidism" in cardiac cases, but the term went out of fashion because it was pointed out that it was the doctor who was masked and signs were there for all to see. That may be so, but they are sometimes confusing, especially when they develop slowly, and what may be obvious to a physician seeing the patient for the first time is not always easy to recognize when one has been attending the patient for several weeks or months. The treatment of thyrotoxic heart failure with anti-thyroid drugs or total ablation of the thyroid gland by radio-active iodine is usually most successful, but requires constant supervision, since excessive amounts of the antithyroid drugs may cause severe myxoedema with recurrence of heart failure.

Conclusion

I think it is fair to say that although recent advances in the treatment of the heart, apart from those contributed by our surgical colleagues, have not been as spectacular as in some other fields, notably the antibiotics, nevertheless there has been a steady gain in knowledge concerning the physiology of the human heart and the reasons why it fails. Cardiac catheterization was the technique for which everyone had been waiting, and the rich harvest is not yet fully gathered in. Meantime we approach the cardiac patient with more understanding and a bigger box of drugs, and our results are better. The patient with heart failure may look ill and may feel very ill, but there is much that we can do, not least by gaining the patient's confidence and dispelling any atmosphere of depression or despair, unjustified even with signs of severe heart failure.

Summary

Digitalis is still the most useful drug in the treatment of heart failure. Many problems remain to be solved regarding its mode of action, but it has been proved by cardiac catheter studies that digitalis is of benefit in all forms of congestive heart failure or left ventricular failure whatever the rhythm. A new drug, procainamide, has proved useful in the treatment of cardiac arrhythmias, but is less successful than quinidine in prophylaxis.

The ultimate result of heart failure is disturbed renal function, and methods of relieving salt retention and oedema are reviewed. Reference is made to the use of oral mercurial diuretics and ion-exchange resins. A new approach to the problem has been suggested by a study of drugs which inhibit the action of the enzyme carbonic acid anhydrase, and preliminary results with "diamox" are described.

The treatment of left heart failure is a medical emergency demanding prompt measures to break the vicious circle causing an overloading of the heart. In addition to the administration of drugs such as morphine and aminophylline, the application of venous tourniquets round the thighs or venesection is advised.

Oxygen is of especial value in the treatment of heart failure caused by chronic respiratory disease, and improved methods of giving oxygen have popularized this form of treatment in the patient's home.

Thyrotoxicosis is a cause of heart failure that is often overlooked, and the response to antithyroid drugs is gratifying.

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CONTROL OF SONNE DYSENTERY IN DAY NURSERIES: A TRIAL OF PHTHALYLSULPHATHIAZOLE

BY A GROUP OF MEDICAL OFFICERS OF HEALTH IN ASSOCIATION WITH THE PUBLIC HEALTH LABORATORY SERVICE SONNE DYSENTERY COMMITTEE*

Sonne dysentery has been and still remains a troublesome infection in day nurseries. In spite of high standards of hygiene the infection often spreads widely. Symptomless excreters are common, and where symptoms are present they are often trivial. Many nurseries, however, accommodate babies, and in view of occasional fatalities among young children the presence of *Shigella sonnei* cannot lightly be ignored.

In an attempt to reduce the time and labour spent in controlling outbreaks of Sonne dysentery in day nurseries, the use of sulphonamides as a prophylactic has been suggested. A study of the published results (see Vollum and Wylie, 1946; Roberts, 1951) and personal inquiry from a number of medical officers of health showed that a number of different drugs in varying dosage have been used. Attempts at chemoprophylaxis were by no means invariably successful, but the results were generally regarded as encouraging.

It therefore seemed desirable to try to establish by a controlled trial whether sulphonamide prophylaxis would limit the spread of dysentery once infection had been introduced among children in a day nursery and whether it would reduce in any way the time and work involved in controlling an outbreak.

Plan of the Trial

Selection of Nurseries.—All day nurseries were included subject to the medical officer of health being satisfied that

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the staff could be relied upon to submit specimens regularly, keep the necessary records, and generally carry out the procedure laid down when an incident occurred.

Definition of Incidents.—An incident was considered to occur when *two or more persons (including the primary case) were found to be infected within one week.*

Selection of Treatment and Control Incidents.—When an incident occurred the medical officer of health consulted a serial list of randomly distributed "treatment" and "control" allocations and allotted the incident to the appropriate group.

Day-to-day Recording.—A form was devised for recording the number of children and staff present in the nursery on each day, the occurrence of diarrhoea, the results of laboratory examinations, exclusions from the nursery, and the administration of chemoprophylactic courses. It was to be filled in continuously during the whole trial.

Procedure for the Investigation of Cases of Diarrhoea.—Any child or member of the staff found to have, or reported as having, diarrhoea, was sent home after a specimen of faeces had been collected, and was excluded until a negative laboratory report had been obtained. All children or members of the staff returning after an absence said to have been due to diarrhoea also had a specimen examined.

When the First Case of Sonne Dysentery Occurred.—Faeces specimens or rectal swabs of all children and staff were collected as soon as possible after the reporting of the first confirmed case. This was generally completed in 48 hours. If the results were all negative and no fresh cases occurred within one week, no further action was taken.

When Two or More Infections Occurred within One Week (an Incident).—If one or more of the faeces specimens yielded *Sh. sonnei* or a second case occurred within one week of the first, the incident was regarded as suitable for inclusion in the trial. The M.O.H. allotted the incident to the "control" or "treatment" group, and further procedure was as follows :

In "control" incidents all infected persons were excluded as soon as the laboratory results were available. Faeces examinations of all persons actually attending the nursery were repeated on the fourth to fifth and eighth to ninth day from the beginning of the incident. All infected persons were excluded from the nursery, and bacteriological examinations continued at weekly intervals until a completely negative "round" was obtained.

All fresh admissions to the nursery were stopped until the incident was closed. All children absent during the incident had one faeces specimen examined when they returned.

In "treatment" incidents all infected persons were excluded as soon as the laboratory results were available. Administration of the sulphonamide to all remaining in the nursery began 48 hours after the faeces or rectal swabs had been collected and continued for five days. Faeces or rectal swabs of all persons were examined seven or eight days from the beginning of the incident (and not less than 48 hours after the cessation of the drug) and thereafter twice weekly until one completely negative "round" had been obtained. All infected persons were excluded as soon as possible.

Suitable arrangements were made for children whose parents refused to allow them to receive the drug, and for absentees. Arrangements were also made for treatment to be continued when necessary over the week-end, when the children did not attend the nursery.

Choice and Dosage of Sulphonamide.—Although Hardy (1946) has shown that the soluble sulphonamides were more effective in the treatment of Sonne dysentery and could be used in much smaller doses than the insoluble sulphonamides, it was decided to choose one of the latter in view of the difficulties of a strict medical supervision of the children while receiving treatment. Phthalylsulphathiazole was used in the dosage shown in Table I. At a later stage

TABLE I.—*Dosage of Phthalylsulphathiazole*

Age (Years)	Daily Dosage	Age (Years)	Daily Dosage
0–	1 g.	4 and 5	2·0 g.
2–	1·5 g.	Adults	3·0 „

of the trial, when it was apparent that the prophylaxis was less successful than had been hoped, the dosage of phthalylsulphathiazole was increased as shown in Table II. Although Ross (1954) reported toxic effects in children with doses no greater than these, no ill effects of sulphonamide treatment were reported.

TABLE II.—*Increased Dosage of Phthalylsulphathiazole*

Age (Years)	Daily Dosage	Age (Years)	Daily Dosage
0–	1 g.	4 and 5	3·0 g.
1–	1·5 g.	Adults	5·0 „
2–	2·5 „		

Results

During the course of the trial, incidents of Sonne dysentery (as defined above) occurred 27 times—13 in the treated series and 14 in the control series.

In Table III are given the numbers of infected children and adults as revealed by the first bacteriological investigation and the numbers of secondary infections revealed by the subsequent examination.

TABLE III.—*Attack Rates: Overall Figures*

	Initial Infection	Secondary Infection
Control series (No. of incidents, 14):		
Adults	6/177 (3%)	1/168 (0·6%)
Children ..	85/593 (14%)	25/472 (5·3%)
Total ..	91/770 (12%)	26/640 (4·1%)
Treated series (No. of incidents, 13):		
Adults	9/173 (5%)	1/175 (0·6%)
Children ..	104/559 (18·5%)	24/438 (5·5%)
Total ..	113/732 (15·5%)	25/603 (4·1%)

In this and the following tables the numerator represents the numbers infected with *Sh. sonnei* and the denominator the total number examined.

In each nursery all the children do not form a single group, but are divided roughly by ages into two or more groups : in a number of instances the infection with *Sh. sonnei* did not occur in one or more of these groups in the nursery, and the overall figures might give a false impression if the infected nursery groups were irregularly distributed. In Table IV the initial and secondary attack rates are given, limited to the group of children infected at the first examination. Again, it will be seen that the incidence of secondary infection was as great in the treated series as in the controls, though it will be seen that the initial infections were rather more frequent in the treated series.

TABLE IV.—*Attack Rates Limited to the Group of Children Infected at the First Examination*

	Initial Infection	Secondary Infection
Control series (No. of incidents, 14)..	85/412 (21%)	24/300 (8·0%)
Treated series (No. of incidents, 13)..	104/401 (26%)	23/294 (7·8%)

The duration of the incident was defined as the time interval from the first confirmed case to the last demonstrated new infection. In the control series this varied from 2 to 21 days, with a mean of 7.7 days ; in the treated series the duration varied from 2 to 18 days, with a mean of 8.5 days.

During the period over which this trial was in operation it was shown by Davies (1954) that a proportion of strains of *Sh. sonnei* in some parts of the country were resistant to sulphonamides. Tests for sulphonamide sensitivity were made, therefore, of strains from the later outbreaks, and

it was shown on two occasions that even the increased dosage of phthalylsulphathiazole did not control infection in nurseries infected with a sensitive strain.

During the course of this trial it became clear that the occurrence of secondary infection could be largely predicted from the proportion of children infected at the beginning of the incident.

In Table V the nurseries in both treated and control groups are divided on the basis of the extent of their infection at the beginning of the incident. When the initial infection was in more than one-sixth of the child population ("high-infection" group), secondary infection occurred in all the incidents in the control and treated groups (the figure of one-sixth was chosen by inspecting the original data—in fact, no nurseries had an initial infection between one-fifth and one-seventh); when the initial infection was limited to less than one-sixth of the children ("low-infection" group), secondary infection was uncommon. It will be seen that these two types of incident were not distributed equally in the two series: the control series had one fewer of the "high-infection" group and two more of the "low-infection" group than the treated series. The rate of secondary infection in the treated series is lower absolutely and in proportion to the initial infection compared with the control series. The difference between the treated and the control series is, however, small compared with the difference between the "high-infection" and "low-infection" groups.

TABLE V.—*Incidence of Secondary Infection in Nurseries Compared with Initial Infection*

Series	Initial Infection in More than One-sixth Total Children			Initial Infection in Less than One-sixth Total Children		
	No. of Incidents	Initial Infection	Secondary Infection	No. of Incidents	Initial Infection	Secondary Infection
Treated	5	79/215 (37%)	21/130 (16%)	8	23/274 (8·4%)	3/281 (1·1%)
Control	4	53/169 (31%)	20/104 (19%)	10	32/414 (7·7%)	5/367 (1·4%)
Total	9	132/384 (34%)	41/234 (17·5%)	18	55/688 (8%)	8/648 (1·2%)

Discussion

The effect of prophylaxis with phthalylsulphathiazole in these day nurseries was very small. This finding does not appear to be due to the occurrence of sulphonamide-resistant strains: the choice of sulphonamide and the dosage, while possibly open to question, was made because it seemed that a wide safety margin was necessary in administering drugs to children in these particular circumstances.

It was found that on two-thirds of the occasions when *Sh. sonnei* was introduced into these nurseries the infection did not spread widely. It will be seen from Table V that in the 18 "low-infection" incidents only 63 persons were infected, an average of less than four per nursery. The close watch for diarrhoea and other suspicious symptoms necessitated by a trial of this kind may have contributed to the unexpectedly large number of low-infection incidents.

The different incidence of secondary infection in the "high-infection" and "low-infection" groups is remarkable and may go some way to explain how such divergent views of the value of sulphonamide prophylaxis have arisen. Thus, of the six day-nursery outbreaks described by Ross (1954) only one would fall into our "low-infection" group, and this was the only outbreak in which he found sulphonamide prophylaxis to appear to be of any value.

It is not possible to say what factors were responsible for "high-infection" and "low-infection" incidents. While it is possible that the former were caused by strains of *Sh. sonnei* with a higher infectivity and were able to spread more rapidly in a day nursery, it seems more likely that, when a high rate of infection was revealed at the beginning of an incident, the infection had been spreading in the nursery unnoticed for some time.

Summary

A controlled trial of prophylaxis of Sonne dysentery in day nurseries using phthalylsulphathiazole has been carried out. The effect of this sulphonamide in preventing secondary infection in the nursery was negligible.

We wish to acknowledge the generous gift of phthalylsulphathiazole used in some nurseries by Messrs. May and Baker Ltd., and the valuable co-operation of the medical and nursing staffs of many day nurseries.

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AUTOGENOUS BACTERIAL VACCINES IN TREATMENT OF ASTHMA

BY

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Bacterial vaccines have been used for many years in the treatment of the infective type of asthma. Different procedures are adopted by different workers. Vaughan and Black (1948) use skin-testing with the vaccine to decide on the dose, Cooke (1947) uses an autogenous vaccine but does not recommend skin tests with it, while Rackemann (1950) believes that the effect of vaccine is non-specific. Yet the general opinion seems to be that in suitable cases, particularly of the infective type of asthma, definite help is obtained from bacterial vaccine therapy.

The trial to be described was undertaken to decide whether an autogenous bacterial vaccine that has been used for a number of years in the asthma clinics at this hospital and elsewhere gives specific help. In attempting a controlled trial of vaccines in asthma we realize that results would be difficult to assess and could easily be misleading in a condition so susceptible to psychological influences. This problem has been discussed by Gaddum (1954) for drug trials in headache such as those carried out by Jellinek (1946), who found that no significant results could be obtained on unselected groups, but that if all those patients who were relieved by blank tablets were excluded a trial could be arranged using the remainder. Such a solution to the problem is impossible among allergic patients, since all of them are to some extent influenced by psychological factors. Even in the case of hay-fever, one of the most clear-cut allergic conditions, 20% of the patients reported improvement on blank tablets in controlled trials of antihistaminics (Frankland and Gorrill, 1953).

It was therefore decided to continue all patients on the treatment that had previously given them the best relief, to advise all of them on diet and environment in the light of skin tests and case histories, and to arrange where necessary for suitable breathing exercises. Thus the pattern of the Medical Research Council chemotherapeutic trials was followed in that the best available

standard methods were given to both groups supplemented either with vaccine or with a control fluid administered in the same way (see Hill, 1951).

Selection of Patients

Only patients with bronchial asthma of an intrinsic type (Rackemann, 1947) were included in the trial, but grossly emphysematous patients as well as those with predominatingly psychogenic and premenstrual asthma were excluded. The patients were selected by two doctors, who continued to review their own cases. Post-nasal swabs or sputum were examined by one bacteriologist (W. H. H.), who prepared a suitable vaccine for each patient. When taken into the trial the patient was given a card with a serial number. All the vaccines with the numbered cards were passed to the statistician (R. H. G.), who placed patients in either the vaccine or the control groups by the use of random number tables. Patients in the control group were issued with carbol-saline instead of the prepared autogenous vaccine. The patients were allowed to have the vaccine changed as often as it was thought necessary, so long as the vaccine passed through statistical control. Not until the completion of the trial and the patient had been fully assessed was it possible for either of the doctors reviewing their patients to know whether the patient had received vaccine or carbol-saline.

Vaccine Treatment

Weekly injections were given, starting with 0.1 ml., and increasing by this amount to 0.5 ml. until first review. The patient then either continued on a maintenance dose, which was often given less frequently than once a week, or the patient had another post-nasal swab or sputum specimen taken and a new vaccine was prepared. The organisms that were considered significant were *Streptococcus viridans* or a non-haemolytic streptococcus when in almost pure culture, any pneumococcus, or *Haemophilus influenzae*, or Friedländer's bacillus. Often there were several types of organism in one vaccine. The equivalent of 0.3 ml. per ml. of a stock vaccine containing per ml. Pneumococcus (mixed types) 50 millions, Friedländer's bacillus 25 millions, Staphylococcus (mixed types) 200 millions, *Bacillus septus* 25 millions, *H. influenzae* 50 millions, Streptococcus 10 millions, and *Micrococcus catarrhalis* 25 millions was added to all autogenous vaccines. The strength of the vaccine was such that it contained 10 million per ml. of each of the autogenous strains.

Method of Assessment

The patients were advised to return for review every fourth month for one year. Table VI shows the numbers returning for 4, 3, 2, or 1 review. The following points were considered: the weight change, the consumption of drugs, the frequency and severity of attacks, the days in hospital, in bed, off work or off school, the general change in incapacity, and the patient's as well as the doctor's opinion as to the general condition following treatment. A system of scoring was used (see Numerical Key), and the final figure from the key gave the final overall result. Although some standard skin tests were performed on all patients and their size was compared each time the patient came up for review, these findings will not be considered in this paper.

Numbers in Trial

The trial was designed to take up to 200 patients for each observer. As only 100 patients were used the control and test groups are of unequal size.

One observer (H.) took 102 patients into the trial and 7 were discarded. The reasons for discarding were: 3 disappeared and could not be traced, 2 died before the trial ended, one developed carcinoma of the lung, and the remaining patient developed pulmonary tuberculosis. Of the 95 patients remaining, 52 were allocated to vaccine treatment and 43 to the control group. Unfortunately, 6 of the patients were not given any injections by their doctor, so that in this series 50 received vaccine and 39 the control fluid.

The other observer (F.) started with 100 patients, and two were discarded, as they could not be traced at the end of the trial. In this series 52 were allocated to vaccine and 46 to the control. However, 3 were not given the injections, and so the numbers are reduced to 50 in the vaccine and 45 in the control group.

Numerical Key for Asthma Survey

	Definition	Score
Original condition and Final condition	Severe continuous	1
	Continuous	2
	Intermittent severe	3
	„ mild	4
	Nil	5
Natural progress of disease	Deteriorating	A
	Constant	B
	Improving	C
Consumption of drugs	Heavy continuous	1
	Regular	2
	Occasional	3
	Nil	4
Weight change	Unintentional loss over 5%	−2
	„ „ „ 2½%	−1
	No change, ±2½%	0
	Slight gain, 2½%	+1
	Definite gain, 5%	+2
	Patients deliberately reducing mark	*
Incapacity	Increased greatly	−4
	„ slightly	−2
	No change	0
	Decreased	+2
	Greatly decreased	+4
Patients' and doctors' opinions	Much worse	−4
	Worse	−2
	No change	0
	Doubtful improvement	+1
	Definite improvement	+2
	Well	+4
Vaccine administration	Continued	A
	Given up	B
	Not given	C

Results

Tables I–V show the distribution of the patients in regard to a number of characters on entry into the trial. While there are differences between the age and marital status of the two main groups, it will be seen that within a group the vaccine and control subgroups are comparable. Table I shows the distribution of all patients who were in the trial at its completion. Tables II–IX show only those who received injections—that is, they exclude the nine patients who did not receive either vaccine or control.

In assessing the results of treatment the grand total of the various factors taken into account has been used (see Table VII). It will be seen that while there is a difference

TABLE I.—*Distribution of Age, Sex, and Marital Status*

Age in Years	H.		F.	
	Female	Male	Female	Male
0–9	0	0	3	8
10–19	6	5	6	16
20–29	14	13	9	4
30–39	13	9	8	0
40–49	11	7	15	3
50–59	8	7	12	6
60+	1	1	3	5

Marital Status	H.	F.
Married	66	49
Single	28	49
Widow	1	0
	95	98

between the two series the vaccine and control groups are similar. The grading of the results is naturally arbitrary, but the results may be grouped as: less than −2 = poor, −2 to +2 = no change, +3 and above = improvement. The data in Table VII have been grouped according to this classification. It will be seen that 54% and 62% (average 58%) improved on the vaccine, while 51% and 54% (average 52.5%) improved on the saline injections.

TABLE II.—*Duration of Asthma in Years, with 0–9 Group Further Subdivided*

Years	H.		F.	
	Vaccine	Control	Vaccine	Control
0–3, 4–6, 7–9 (0–9)	10, 6, 11 } 27	6, 8, 5 } 19	13, 5, 11 } 29	9, 7, 6 } 22
10–19 ..	15	10	11	13
20–29 ..	5	8	5	7
30–39 ..	1	2	3	2
40+	2	0	2	1
All ages ..	50	39	50	45

TABLE III.—*Original Condition. See Numerical Key for Coding*

	H.		F.	
	Vaccine	Control	Vaccine	Control
Severe continuous (1) ..	1	0	2	3
Continuous (2)	12	13	21	15
Intermittent severe (3) ..	23	19	16	21
,, mild (4) ..	14	7	11	6
	50	39	50	45

TABLE IV.—*Drug Consumption at Start of Trial*

	H.		F.	
	Vaccine	Control	Vaccine	Control
Heavy continuous (1) ..	6	5	4	6
Regular (2)	28	24	29	23
Occasional (3)	9	5	15	15
Nil (4)	7	5	2	1
	50	39	50	45

TABLE V.—*Natural Progress of the Disease*

	H.		F.	
	Vaccine	Control	Vaccine	Control
Deteriorating, A	20	13	17	17
Constant, B	30	26	33	28
Improving, C	0	0	0	0
	50	39	50	45

TABLE VI.—*Follow-up*

No. of Times Seen	H.		F.	
	Vaccine	Control	Vaccine	Control
4	35	29	47	43
3, 2	12	8	3	2
1	3	2	0	0
	50	39	50	45

TABLE VII.—*Results of Treatment*

Score	H.		F.	
	Vaccine	Control	Vaccine	Control
−11, −7–10, −3–6 Worse ..	0, 1, 5 } 6	2, 1, 2 } 5	5, 3, 4 } 12	1, 1, 8 } 10
−2, +2 No change ..	13	13	11	12
+3+6, +7+10, +11 Improved ..	10, 16, 5 } 31	8, 9, 4 } 21	9, 15, 3 } 27	1, 14, 8 } 23
	50	39	50	45

TABLE VIII.—*Comparison of Patients Who Completed (A) With Those Who Defaulted from (B), the Vaccine Course*

Score	H.				F.			
	Vaccine		Control		Vaccine		Control	
	A	B	A	B	A	B	A	B
Less than −3 ..	1	4	2, 11	3	7	5	4	6
−3, +3	11	3		4	10	2	12	1
More than +3..	25	6	16	3	23	3	20	2
	37	13	29	10	40	10	36	9

TABLE IX.—*Results of Treatment by Duration of Disease*

Duration in Years	H.				F.			
	Vaccine		Control		Vaccine		Control	
	0–9	10+	0–9	10+	0–9	10+	0–9	10+
Score less than −3	3	2	3	2	5	7	4	6
−3, +3	8	6	6	9	9	3	5	8
More than +3 ..	16	15	10	9	16	10	13	9

In an attempt to determine any factors that might influence the results, those who stopped having injections (Group B) were compared with those who took the full course (Group A) (Table VIII). The grouping has been widened to allow for the smaller numbers. It will be seen that, comparing A and B in each subgroup, the patients who gave up vaccine injections fared worse than those who took the whole course. It would be interesting to know if there is any character which allows recognition of a "B" patient before treatment is begun. Despite extensive analysis no positive results in this direction were obtained, and the tables concerning these are therefore omitted.

The relationship of duration of asthma to the final grading was also investigated, and is shown in Table IX, where it will be noted that the duration of the disease had surprisingly little effect on the results.

Finally, there is the small group of patients who failed to receive any injections whatever. Their scores were: (H.), −4, −3, 0, +1, +4, +10; (F.), 0, +5, +8; that is, using our original standard 2 gave poor result, 3 were unchanged, and 4 were improved.

Discussion

This trial was devised to see whether an autogenous bacterial vaccine, as usually given to the intrinsic type of asthma as specific prophylactic therapy, produced any greater benefit to the patient than carbol-saline injections. The selection of the patients might well have been biased in some way, though it was hoped that this factor would be offset by the division of the trial under two doctors, one of whom believed that a bacterial vaccine helped specifically, while the other considered that any improvement was quite incidental to vaccine therapy. The number of injections of the vaccine used by the two doctors, and its strength, differed to some extent, so that each saline control group as well as the total in each group served as a control for any difference in the details of vaccine therapy. Although the results have been given separately in the tables, the pooled results can be considered together. It will be seen that 58% showed improvement on the bacterial vaccine, while 52% showed improvement on the carbol-saline.

Conybeare and Knott (1936) noted, in their series of asthmatic patients treated with bacterial vaccines, that if many of the patients were mild asthmatics, particularly of a short duration, any kind of treatment tended to show a high percentage of improvement. They suggested that the lack of preliminary grading in severity of asthma had led to the great variation in the reported results from the use of vaccines. In this trial, grading of asthma, although carried

out, has not been given in detail because the number of the severe asthmatics under treatment is not large enough for statistical evaluation. Even so, among the severe asthmatics no greater number were helped by an autogenous vaccine than by the carbol-saline. This is further evidence that, under the conditions in which the vaccine was given, any benefit obtained is apparently non-specific in effect.

The trial shows that the ordinary palliative measures, combined with the psychological support supplied by a weekly visit to and injection by the patient's own doctor, are capable of giving prolonged benefit to half the patients. It may therefore be assumed that in asthma any result that does not show a statistically significant improvement on a figure of 50% relieved does not support the value of any allegedly specific therapy.

It must, however, be pointed out that although this trial did not show any statistically significant difference between autogenous vaccine therapy and saline injections in the treatment of asthma, it does not necessarily follow that bacterial vaccines may not be of specific benefit in the treatment of asthma. No attempt was made here to compare different strengths or qualities of vaccines or the spacing of the injections, or other possible variables in vaccine therapy.

Summary

In a controlled trial in some 200 cases of intrinsic (infective) asthma, kept under observation for one year or more and given general supportive treatment, regular injections of autogenous bacterial vaccines produced no greater benefit to the patients than similar injections of carbol-saline. In both groups over 50% of the patients benefited from the treatment received.

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ANTICOAGULANT STUDIES WITH "MARCOUMAR," A NEW COUMARIN DERIVATIVE

BY

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"Marcoumar" (3-(1'-phenylpropyl)-4-hydroxycoumarin) is a synthetic anticoagulant. The initial clinical investigations with this drug have shown that it is highly active, with a prolonged anticoagulant action (Koller and Jakob, 1953). Like dicoumarol and ethyl biscoumacetate it has a greater effect on the concentration of factor VII (stable prothrombin accelerator) than on the actual prothrombin concentration of the plasma, while it exerts very little effect on the concentration of factor V (labile prothrombin accelerator) present in the plasma. Koller and Jakob considered that estimation of the "prothrombin complex" by the one-stage Quick method, using a suitable brain preparation as source of thromboplastin, was adequate for clinical control of the drug.

Marcoumar has been used widely on the Continent, and a number of workers have reported favourably on its use in the treatment of acute thrombo-embolism and in cases requiring long-term anticoagulant therapy. Control of dose was achieved with weekly or twice-weekly prothrombin-time estimations in the long-term cases (Aldehoff and Weidenbach, 1954; Matis, 1953; Deutsch *et al.*, 1954).

The following advantages have been claimed for the drug: (1) Freedom from toxic reactions. (2) A definite effect on prothrombin time within 24 hours, while a therapeutic level is obtained within 36 to 48 hours. (3) A prolonged stable action, allowing good control with a single daily dose, and a gradual return of the prothrombin time to normal once treatment is stopped. (4) Less effect on capillary fragility than certain other anticoagulant substances. This effect has been shown experimentally (Jürgens, 1953; Matis, 1953) and may be a factor in the development of haemorrhage when estimations of the prothrombin time or factor VII content are within the accepted therapeutic range.

The development of vitamin K_1 has been the most important factor allowing therapeutic use of the long-acting anticoagulants. This substance, now available in oral form, will revert a prolonged prothrombin time to a safe level within two to six hours and can be used at the first sign of haemorrhage, or prophylactically should the prothrombin concentration fall to low levels.

The purpose of this paper is to report experience with the use of marcoumar in 100 patients. Their ages ranged from 37 to 89 years.

The conditions for which patients were treated are shown in Table I.

TABLE I

	No. of Cases	Mortality
Cardiac infarction	73	13
Post-operative thrombophlebitis	10	—
Spontaneous thrombophlebitis	8	—
Retinal vein thrombosis	2	—
" artery "	1	—
Pulmonary embolus	3	—
Recurrent cerebral thrombosis	1	—
Temporal arteritis	1	1
Rheumatic heart disease	1	—

Methods

Prothrombin times were measured by the one-stage method of Quick, using brain as a source of thromboplastin.

Prothrombin times were taken in the majority of patients before starting treatment, and this influenced the initial dose given if the prothrombin concentration was below normal. Prothrombin times were estimated each morning, except Sundays, throughout this study. In those who continued as out-patients, weekly or twice-weekly times were estimated. Careful inquiries were made for a history suggesting chronic peptic ulceration, or chronic renal or hepatic disease, but it was not found necessary to exclude any cases on these counts in the present series.

Dosage.—Marcoumar is supplied in 3-mg. tablets which are readily divided. Most patients received from 18 to 21 mg. on the first day and 9 to 12 mg. on the second day. If the initial prothrombin concentration was below 55% a smaller initial dose was given. The maintenance dose depended on the daily prothrombin time, and throughout the study the aim has been to keep the prothrombin time at two to two and a half times that of the control, which is equivalent to a prothrombin concentration of between 25 and 15%.

Heparin was given four-hourly for the first 36–48 hours in most cases until the prothrombin time was shown to be within the therapeutic range.

Results

Rapidity of Action.—The majority of patients showed a clear fall in prothrombin concentration after 12 to 16 hours and reached a therapeutic range within 36 hours. Fig. 1

illustrates the effect in a patient who was given marcoumar without heparin and shows a fall to 36% within 14 hours and to 15% 38 hours after the first dose.

Duration of Effect.—In all cases in which it has been studied the prothrombin concentration has taken a number of days to return to normal after treatment had been stopped. This has varied from 9 to 14 days (see Fig. 2).

Control Achieved.—Patients have been treated for periods ranging from several days to seven weeks. Some continued to receive the drug on a long-term basis as out-patients. In an attempt to assess the control achieved the number of days in which the prothrombin concentration was over 30% after the third day of treatment has been noted. The overall stability of the prothrombin concentration from day to day has also been taken into consideration, and undue swings, even if the prothrombin concentration remained below 30%, have been regarded unfavourably. On this basis the graphs of patients have been classified as good, fair, or poor. The control was good in 76 cases, fair in 19, and poor in 2. Three patients who died within four days have been excluded. In the whole series the prothrombin concentration exceeded 30% after the third day of treatment on 58 occasions out of a total of 1,854 days, which gives an incidence of 3%. On 20 occasions the prothrombin concentration was less than 10%, which gives an incidence of 1%. Fig. 3 is a graph representative of the "good" control group.

Maintenance Dose.—This has varied considerably from case to case and sometimes in the same case, and can be assessed in each individual only by frequent estimations of the prothrombin time in the first two weeks of treatment.

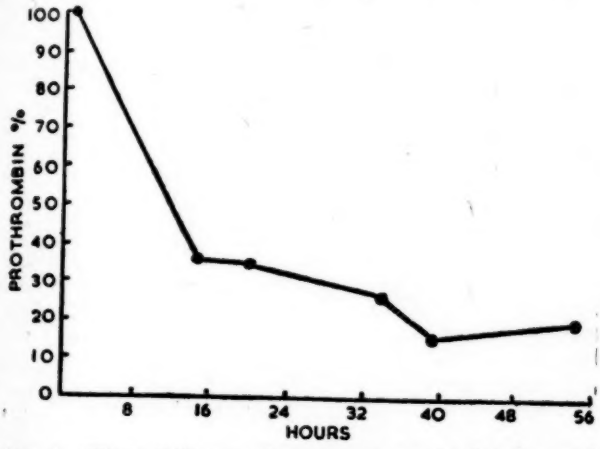

FIG. 1.—Effect of 21 mg. of marcoumar on the first day, and 9 mg. after 22 hours, in a patient with coronary insufficiency. No heparin was given.

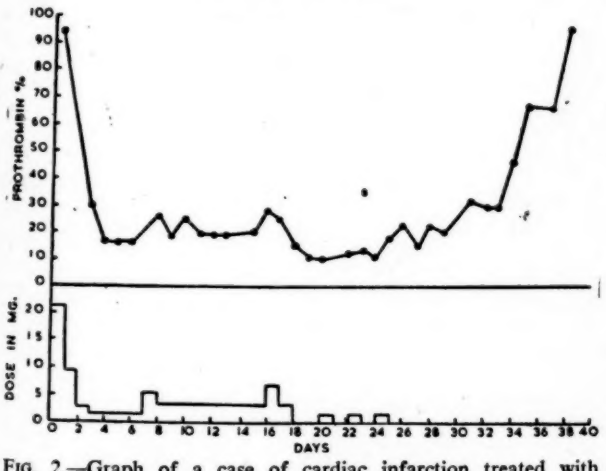

FIG. 2.—Graph of a case of cardiac infarction treated with marcoumar. The gradual return of prothrombin concentration to normal after stopping treatment is shown.

It was found that in severely ill patients a smaller initial and maintenance dose was required until clinical improvement took place, when a larger dose was often required to maintain control. Following the initial dose on the first two to three days the maintenance dose was often small, and in some cases no marcoumar was required for two to five days. The average case required 1.5–3 mg. daily to maintain control; a small number of cases needed as much as 4.5–7.5 mg., and appeared relatively resistant to the drug.

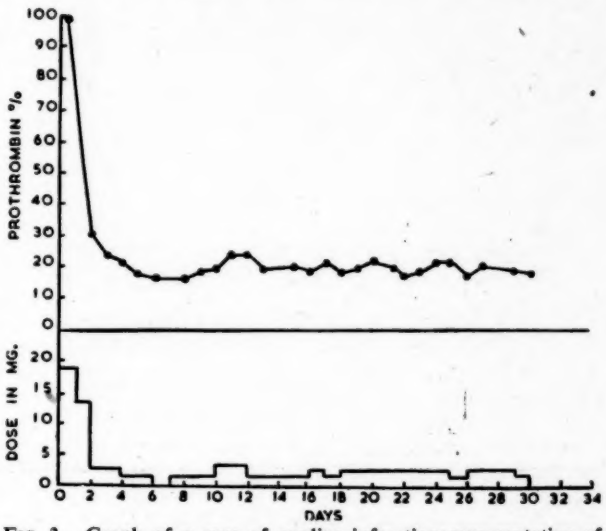

FIG. 3.—Graph of a case of cardiac infarction representative of the "good" control group.

The maintenance dose was noted to be greater in one patient during a bout of epidemic diarrhoea, when absorption may have been less adequate. In the early stages of the investigation one-quarter of a tablet (0.75 mg.) was sometimes given; it has since been found that 1.5 mg. given at less frequent intervals produced just as stable a result and avoided difficulties in dividing tablets into quarters.

Side-effects.—In one patient the drug appeared to cause some mild diarrhoea, which improved when treatment was stopped. No other side-effects were noted.

Thrombotic Complications.—Undisputed evidence of thrombo-embolus occurred in five cases. One patient with Hodgkin's disease developed an extension of a superficial thrombosis while on treatment; one patient had a cerebral embolus believed to arise from a mural thrombus, and three patients had pulmonary emboli on the second, third, and fifth day after starting treatment respectively. Three cases of cardiac infarction had an extension of their infarct and five had continued pain while on treatment. These latter were regarded as doubtful cases of further thrombosis.

Haemorrhagic Complications.—Haemorrhage occurred in 10 patients—an incidence of 10%. In only five did it cause any concern, and in one of these it may have contributed in some way to the patient's death. This patient, aged 80, had severe hypertension and temporal arteritis with coronary arteritis, and died of a massive cerebral haemorrhage. The prothrombin concentration on the day before death was 18% and control had been excellent. Anticoagulants were given in order to lessen the risk of blindness developing. Necropsy confirmed the clinical diagnosis and showed gross cerebral arteriosclerosis with an extensive cerebral haemorrhage. The hypertension and cerebral vessel changes made it unlikely that marcoumar affected the outcome in any way. Haematuria, epistaxis, and haemoptysis each occurred in different patients (Table II) and were not severe. The haemoptysis was thought to arise from ulceration of the bronchus in a patient with stenosis of the lingula lobe bronchus. One patient had a very slight bleeding per rectum from haemorrhoids. This patient had noted similar trouble before admission, and no special treatment was given, nor

were the anticoagulants stopped. In one patient a small secondary haemorrhage occurred from an operation wound on the ninth day.

TABLE II.—*Haemorrhagic Complications*

Site of Haemorrhage	Prothrombin Concentration at Time of Bleeding	K_1 Given
Epistaxis	12%	Yes
"	16%	No
"	17%	Yes
"	18%	No
Haematuria	25%	No
"	10%	Yes
Cerebral haemorrhage	18%	No
Haemoptysis	23%	Yes
Bleeding per rectum	21%	No
Haemorrhage into wound	24%	No

Discussion

The important criteria in the evaluation of any prothrombin depressant are safety, effectiveness, economy, and convenience of administration. Marcoumar would appear to fulfil these to an extent at least similar to or greater than some of its predecessors.

The important claims made for it have been supported by the present investigations. It is a potent substance which produces its effects more quickly than dicoumarol. The induction rate of marcoumar is between 24 and 48 hours, while that of dicoumarol lies between 48 and 72 hours. This rapid action gives the drug an important advantage over dicoumarol, allowing rapid restoration of the prothrombin concentration to within the therapeutic range should it show an unexpected rise during the course of treatment. Under these circumstances it is often 24 to 36 hours before a larger dose of dicoumarol exerts its effect, whereas in our experience a suitable dose of marcoumar will restore the prothrombin concentration within 12 to 18 hours and so allow smoother control.

Patients receiving the drug are readily controlled within the therapeutic range and are easily maintained within that range over a period of time. It has been found that seriously ill patients have required lower doses until their general condition improved, daily estimations of the prothrombin concentration being necessary during this phase. In some such patients initial doses of 18 and 9 mg. on the first and second days have been sufficient to maintain the prothrombin concentration at around 15–18% of normal for as long as four to six days; with clinical improvement the maintenance dose has been increased and daily doses varying from 1.5 to 3 mg. have been necessary.

The recovery period on stopping marcoumar therapy is longer than with dicoumarol, but this is not a disadvantage. If a rapid return towards normal is required for unexpected surgery, in the case of an injury, or when an unusually low prothrombin concentration and bleeding occur, then oral vitamin K_1 may be given. The development of a cheap oral K_1, which neutralizes the effect of the drug very rapidly, has removed all objections to long-acting anticoagulants and lessened very greatly the dangers of haemorrhage in response to such drugs.

Observations made during the present investigation confirmed that restoration of prothrombin concentration to a safe level occurred within four to six hours of an oral dose of 10–20 mg. of vitamin K_1.

Some evidence of haemorrhage occurred in 10 cases in the present series. In the elderly patient in whom a fatal cerebral haemorrhage occurred the necropsy showed severe cerebral atheroma and an extensive cerebral haemorrhage. Anticoagulants may not have contributed significantly to the fatal outcome in this patient, although cases of severe hypertension and arteriosclerosis may be expected to be more liable to retinal or cerebral haemorrhages when on anticoagulants, and the risks must be carefully assessed in such cases.

In only one of the remaining patients who showed evidence of haemorrhage was it found necessary to stop treatment and give vitamin K_1; this patient, who was being treated for coronary insufficiency, had small haemoptyses from a post-tuberculous bronchostenosis with ulceration, and the bleeding occurred when the prothrombin concentration was 23% of normal. In three other cases vitamin K_1 was given and treatment continued when bleeding had stopped.

The incidence of further thrombo-embolic episodes has been small in the series, clear evidence of thrombo-embolism occurring in five cases. In two of these it appeared on the second day of treatment before full control had been achieved and while the patients were on heparin in addition to marcoumar.

The indications for long-term ambulant anticoagulant therapy are well recognized in certain cases of recurrent thrombophlebitis, in thrombophlebitis migrans, and in certain cases of mitral valve disease which have suffered repeated embolic accidents; the indications in peripheral vascular disease and in coronary artery disease are less well defined, but may include some cases of recurrent cardiac infarction. The therapeutic level which should be aimed at in such ambulant patients is a matter of some debate, but probably lies between 20 and 25% of the normal prothrombin concentration. The availability of long-acting stable anticoagulant substances, whose action may be quickly reversed by vitamin K_1, has made ambulant anticoagulant therapy relatively safe for the patient and easily controlled by the physician who has good laboratory facilities available. The value of such therapy will be known only when the results of carefully controlled observations made over a considerable period of time are available.

Summary

Marcoumar (3-(1'-phenylpropyl)-4-hydroxycoumarin) has been used in the treatment of 100 patients suffering from conditions considered to require anticoagulant treatment.

It is a potent oral anticoagulant substance which reduces the prothrombin concentration to a therapeutic level within 36 to 48 hours, while some effect may be demonstrated within 12 hours of an oral dose.

The maintenance dose varies from patient to patient and at times in the same patient, and is less in severely ill persons. In the majority of subjects the maintenance dose becomes stable, and good control in out-patients has been achieved with small daily doses and prothrombin estimations every fourth to seventh day.

Marcoumar has a prolonged action and the recovery period has varied from 9 to 14 days. This recovery has been shown to be very materially accelerated by oral vitamin K_1, should it be necessary in the event of haemorrhage.

Bleeding occurred in 10 patients. One elderly patient with severe hypertension and temporal arteritis died of a cerebral haemorrhage. The bleeding in the remaining patients was mild, and vitamin K_1 was given on four occasions.

No other toxic effects were observed, and it is concluded that marcoumar is a satisfactory long-acting anticoagulant which is stable, easy to control, and suitable for both short-term and long-term anticoagulant therapy.

I wish to acknowledge the help received from the physicians and surgeons of the Wellington Hospital who have allowed me to supervise the anticoagulant control of patients under their care, and to the laboratory staff for their very careful attention to the prothrombin estimations. I am grateful to Roche Products Limited, who generously provided the "marcoumar" and vitamin K_1 ("konakion") used in this trial.

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PROTHROMBIN PATTERN OVER THE 24 HOURS IN PATIENTS RECEIVING ORAL ANTICOAGULANTS

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Much is known about daily prothrombin concentration in patients receiving oral anticoagulants,* but we can find no published observations on prothrombin levels at shorter intervals. The purpose of this investigation was to determine the variation of prothrombin concentrations throughout the 24 hours.

Methods

Nineteen patients were studied (17 males and 2 females); 9 had myocardial infarcts, 4 coronary insufficiency, 3 venous thromboses in the leg, and 3 pulmonary embolisms. Ten patients received phenindione (" dindevan ") and 9 ethyl biscoumacetate (" tromexan "). All prothrombin estimations were made by one of us (E. G. W.), using Quick's one-stage method. The anticoagulant was given as a single dose at 6 p.m., and blood specimens were taken two-hourly from 6 p.m. until 6 p.m. the following day. The interval between the start of treatment and the 24-hour test period varied from patient to patient.

Results

The two-hourly prothrombin concentrations are expressed as a percentage of normal in Tables I and II. The mean prothrombin level at each two-hourly interval is shown separately for ethyl biscoumacetate and phenindione in Fig. 1. Patients on ethyl biscoumacetate had an average prothrombin level about 10% higher than those on phenindione therapy, a purely adventitious difference which persisted throughout the experiment. Nevetheless, the overall effect is similar for both preparations, showing a small initial rise followed by a gradual and progressive decline until about noon, when the level begins again to increase. The trend probably represents a progressive depression of prothrombin level by the anticoagulant until its effect begins to wear off. We do not know whether the prothrombin level has a diurnal rhythm in a normal individual, but it is unlikely that a picture which conforms

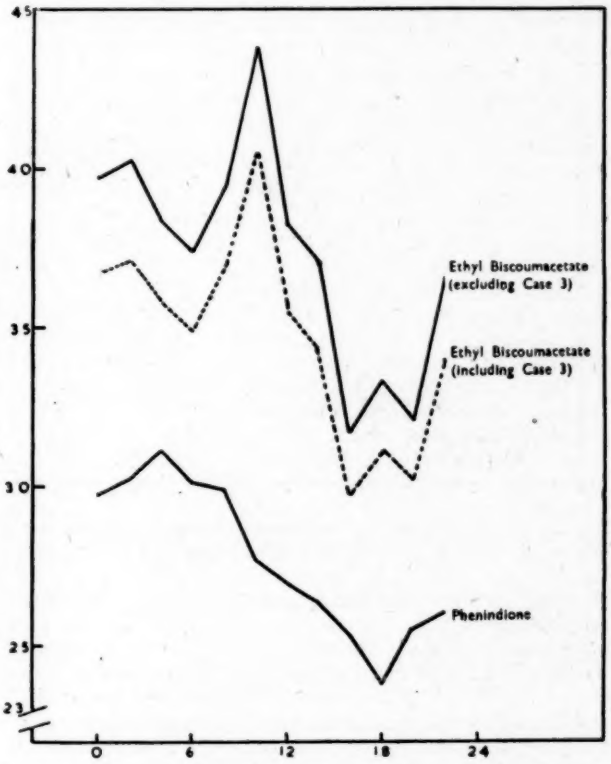

FIG. 1.—Mean prothrombin level. Abscissa: hours after administration of anticoagulant. Ordinate: per cent. normal prothrombin.

TABLE I.—*Phenindione. Two-hourly Prothrombin Concentrations Expressed as Percentage of Normal*

Case	6 p.m.	8 p.m.	10 p.m.	12 p.m.	2 a.m.	4 a.m.	6 a.m.	8 a.m.	10 a.m	Noon	2 p.m.	4 p.m.	6 p.m.	
1. Myocardial infarct. .	29	29	32	32	27	27	26	23	21	21	26	25	26	
2. " " ..	28	26	26	24	25	24	24	24	24	21	24	22	—	
3. " " ..	34	34	31	34	31	28	28	28	31	28	29	34	34	
4. Vein thrombosis ..	23	22	22	21	28	26	21	22	20	18	17	18	17	
5. " " ..	18	20	22	20	20	18	20	20	19	21	20	20	20	
6. Pulmonary embolus. .	24	25	28	28	20	20	15	18	15	15	15	15	18	
7. Coronary insufficiency	20	23	25	27	37	25	26	31	24	23	22	22	30	
8. Myocardial infarct ..	40	40	38	45	38	40	40	30	30	26	32	32	28	
9. " " ..	42	38	42	36	33	33	36	34	38	34	36	38	34	Optimum range 10–30%
10. " " ..	40	45	45	34	40	36	34	34	31	31	34	34	—	

TABLE II.—*Ethyl Biscoumacetate. Two-hourly Prothrombin Concentrations Expressed as Percentage of Normal*

Case	6 p.m.	8 p.m.	10 p.m.	12 p.m.	2 a.m.	4 a.m.	6 a.m.	8 a.m.	10 a.m.	Noon	2 p.m.	4 p.m.	6 p.m.	
1. Coronary insufficiency	55	50	55	50	50	55	36	40	40	42	40	40	40	
2. " "	36	45	40	36	24	32	29	34	27	29	31	30	36	
3. Myocardial infarct ..	12	12	16	15	16	14	14	14	14	14	15	14	17	
4. Coronary insufficiency	31	40	28	32	47	52	56	47	38	30	25	40	40	
5. Myocardial infarct ..	54	50	30	40	50	50	48	48	31	48	43	48	50	
6. Pulmonary embolism. .	45	42	45	34	48	58	40	40	42	40	44	40	38	
7. " " ..	37	36	37	37	31	38	32	28	23	27	24	39	34	Optimum range 10–30%
8. Vein thrombosis ..	29	29	36	34	31	29	29	28	25	23	23	26	28	
9. Myocardial infarct ..	31	30	36	36	34	36	36	31	28	27	27	27	26	

so well to expectation would also correspond so closely to a natural rhythm, or would show so wide a range of variation.

On average the ethyl biscoumacetate group showed a wider variation of prothrombin over the 24 hours than the phenindione group, four patients treated with ethyl biscoumacetate having a range of variation greater than 20%, whilst the greatest range among patients on phenindione was 19%. The variability of the two groups is compared in Fig. 2, where the standard deviation of the readings obtained at each interval of two hours is plotted against time. As in Fig. 1, the ethyl biscoumacetate figures are drawn both including and excluding one case with an unusually low prothrombin level. The only noticeable difference between

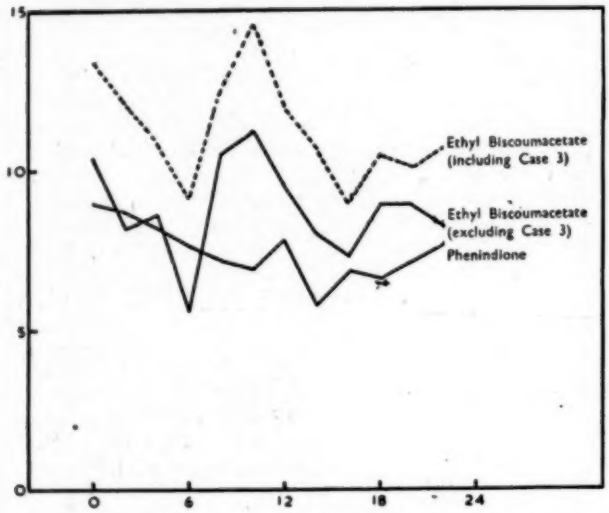

FIG. 2.—Standard deviation. Abscissa: hours after administration of anticoagulant. Ordinate: per cent. normal prothrombin.

phenindione and ethyl biscoumacetate is a vertical shift of the curve; the general shape remains unchanged, and each patient shows broadly the pattern of response exhibited in the mean curves of Fig. 1. The ethyl biscoumacetate group does not differ greatly when the aberrant case is excluded.

When allowances are made for differences between individuals and differences in times of day, the residual variation—attributable to uncontrolled factors and errors of determination—is small, amounting to a standard deviation of just over 3% in the phenindione group and about 5½% in the ethyl biscoumacetate group.

Conclusions

An experiment of this kind is laborious and involves considerable inconvenience to the patient. The number of observations has therefore been limited, but the following conclusions may be drawn.

1. Anticoagulants of the ethyl biscoumacetate and phenindione type are effective when given in a single daily dose as soon as the patient is considered to be stabilized.

2. The prothrombin concentration remains at a relatively high level for 8 to 10 hours after administration of the anticoagulant, and falls progressively to its lowest level after about 18 hours.

3. Blood for prothrombin estimations should be withdrawn from any individual patient at approximately the same time of day.

4. Although our investigation has shown a difference in response to the two anticoagulants, our observations are not sufficient to allow an appraisal of their relative merits.

A CASE OF ACUTE PHLEGMONOUS CAECITIS WITH PERFORATION

BY

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Acute phlegmonous caecitis is still regarded as a rare disease, and the condition is not described in standard textbooks. Only approximately 40 cases have so far been reported in the medical press, and most reports originate from practitioners in the U.S.A. The first case of phlegmon of the large intestine was reported by Goldschmidt (1887). Later on Hallopeau and Monod (1919) described the condition under the heading, "Gangrène massive du Caecum." Hagler (1920) reported a case of a dissecting interstitial abscess of the caecal wall. A case of ruptured gangrenous caecum in a child of 8 was reported by Rose (1932). Cox (1944) published two cases of acute gangrene of the caecum. Spivack and Busch (1943) reported two further cases of phlegmonous caecitis. A case of the same condition in a man aged 35 is described by Meyer and Disch (1945); further cases have been reported by McHardy and Browne (1946), Bulmer (1947), Riker, Gilchrist, and David (1949), and Nardell (1949); and Tagart (1953) surveys 21 cases reported during the last 25 years with three further cases.

Pathology

Two types of phlegmonous caecitis have been described by most authors, circumscribed and diffuse. A normal appendix is found in all cases, except when the appendix has become inflamed by contiguity. There are, however, distinct signs of an inflammatory lesion in the right iliac fossa, and, according to the type of the disease, there may be a well-defined thickening of the caecal wall or diffuse induration of the entire caecum. The affected area shows signs of acute inflammation, and ulcers penetrating as far as the serous coat have also been described. Gangrene with perforation and general peritonitis occurred in the case to be reported. On many occasions the lesion has been mistaken for carcinoma. The microscopical picture consists of infiltration by polymorphonuclear leucocytes in the submucosa and to a less extent in the subserosa, muscularis, and mucosa. According to Spivack and Busch the lesion is said to begin as a cellulitis of the submucosa. Streptococci and staphylococci, but also *Bact. coli* and pneumococci, have been isolated, and most authors agree that bacterial invasion of the submucosa following trauma by hard faeces, foreign bodies, fruit stones, or parasites is the most likely cause of phlegmonous caecitis. As additional causes anatomical abnormalities such as a mobile caecum with stasis have been suggested. The possibility of a haematogenous portal of entry has been stressed by Spivack and Busch.

Clinical Features

Most cases of acute phlegmonous caecitis have been diagnosed either as acute appendicitis or as appendix abscess. Most authors agree that a mass appearing in the right iliac fossa early, even in the first 48 hours, may be indicative of the condition. The disease has occurred in children and adults, and it is no more frequent in males than in females. The history is usually short. The diagnosis in the case reported below was made difficult by the fact that the patient was admitted in a diabetic coma. A precise history could not be obtained, and the symptoms of advanced peritonitis became obvious only when the patient started to regain consciousness. A mass could not be palpated.

In the differential diagnosis, in addition to acute appendicitis and appendix abscess, tuberculosis of the caecum, carcinoma, volvulus, and regional enteritis have to be considered.

Treatment and Prognosis

Because of the difficulty in arriving at a correct diagnosis laparotomy is essential at the earliest opportunity. The course of treatment to be taken will largely depend on the type and stage of the disease. Acute phlegmonous caecitis has a tendency to subside and to resolve, but, on the other hand, it may spread and progress to gangrene and perforation with peritonitis. It has been suggested that some cases of appendicitis or of appendix abscess, treated conservatively, may have been cases of phlegmonous caecitis which had resolved without leaving clinically or radiologically traceable sequelae. If a case of circumscribed phlegmonous caecitis without gangrene or perforation has been found at operation, removal of the lesion seems unjustifiable. Closure of the abdomen with or without drainage, followed by adequate chemotherapy, would appear to be the correct treatment for such cases. In the case of imminent perforation Tagart suggests excision of the diseased area and closure of the resulting defect in layers, or suture of the area to the anterior parietal peritoneum. Ileo-caecal resection is recommended by Spivack and Busch for the diffuse type of phlegmonous caecitis or if carcinoma cannot be ruled out. In the case reported below perforation of a circumscribed gangrenous portion of the caecal wall had occurred. The gangrenous area was excised and the resulting defect was used as a caecostomy. Because of general peritonitis the peritoneal cavity was drained.

The mortality in uncomplicated cases of acute phlegmonous caecitis is said to be in the region of 8%; 45% if the lesion is not limited to the caecum.

Case Report

A married woman aged 23, a diabetic whose condition it had been difficult to control, was admitted to hospital on October 28, 1954. According to her doctor she had been in a coma for the last six hours, and, in view of her previous history, diabetic coma was diagnosed on admission. The usual regime for diabetic coma was begun immediately. It was also found on admission that she was bleeding from her vagina and was having an incomplete abortion. On October 30, two days after admission, she was still semiconscious, but her general condition had somewhat improved. Her pulse, which had been imperceptible on admission, showed better volume and she appeared generally more responsive. On November 2 she seemed to complain of abdominal pain and she vomited large amounts of bile-stained fluid. She showed signs of an acute abdomen, and a surgical opinion was sought. The patient when seen by me appeared to be extremely ill; her temperature was subnormal and the pulse rapid and of poor volume. She looked toxic, her tongue was dry, and she seemed to be dehydrated. Examination was very difficult because of her only partial response to questioning. The abdomen was distended and generally tender, and there was guarding and release tenderness in the entire lower abdomen. Bowel sounds were absent and there was no palpable mass. Rectal examination was inconclusive. A slight loss occurred vaginally, the external os admitted the finger-tip, and the internal os was closed. It was impossible to make out the size of the uterus because of her abdominal rigidity and distension. Blood sugar at the time of examination was 112 mg. per 100 ml.; blood urea, 137 mg. per 100 ml.; CO_2 combining power, 14.6 mEq/l. There was a trace of sugar in her urine, but no acetone.

Paralytic ileus due to general peritonitis, the cause of which was obscure, was diagnosed and laparotomy was decided upon.

First Operation.—Laparotomy was performed on November 2, under general anaesthesia (thiopentone; pethidine, 30 mg.; D-tubocurarine chloride, 10 mg.; gas and oxygen). A right lower paramedian incision was made, and on opening the peritoneal cavity a large quantity of thick yellow pus welled up. Advanced general peritonitis was found; almost the entire small bowel was distended and caked together, with pockets of pus between the loops. It was impossible on first sight to detect the primary cause of the peritonitis. The appendix was found to be normal; on closer inspection of the caecum a round patch of gangrene, 2 in. (5 cm.) in diameter, was discovered on the outer caecal wall. The affected part of the caecum was almost black, the tissues had begun to disintegrate, and there was a small perforation in the centre of the lesion through which the intestinal contents could be seen to ooze. The lesion was strictly circumscribed and there was no induration of the surrounding tissues. Apart from a few enlarged glands in the ileo-caecal angle and an enlarged uterus, no further abnormality was noticed. There was no sign of a foreign body near the lesion.

The patient's condition had steadily deteriorated during the operation, her pulse had become imperceptible, and when the cause of the peritonitis had become obvious she was practically moribund. The gangrenous part of the caecal wall was quickly exteriorized, the gangrenous area was excised with diathermy, and the remaining opening was used as a caecostomy into which Paul's tube was tied. The peritoneal cavity was drained through the original incision.

Post-operative Course.—After her return to the ward the patient's condition seemed to have slightly improved. Intravenous 5% glucose in physiological saline, which had been started during the operation, was continued together with intravenous chlortetracycline, 250 mg. four-hourly, gastric suction was instituted, and the diabetes was supervised by the physicians. By November 5 her condition had much improved; intravenous drip therapy and gastric suction were discontinued, and chlortetracycline, 250 mg. orally, was given. She was fully conscious from the second post-operative day, the caecostomy was acting satisfactorily, and by November 15 the paramedian wound was healed. From then her convalescence was quite uneventful; her diabetes seemed fairly well controlled, the caecostomy was acting less every day, and she started to have normal bowel actions. Because of considerable skin irritation round the caecostomy, which by December 2 had become stationary, it was decided to close the opening by operation.

Second Operation.—Closure of the caecostomy was carried out on December 6. The caecum was dissected out with considerable difficulty because of dense adhesions, and closed in layers intraperitoneally. Her convalescence was again uneventful, and she was discharged healed on December 23. She has been seen fortnightly at the surgical and medical out-patient clinics since; her diabetes is fairly well stabilized and her general condition is quite satisfactory.

The pathologist's report on a swab taken during laparotomy on November 2 stated: Cultures have yielded a growth of coagulase-positive *Staph. aureus*, sensitive to penicillin, streptomycin, chloramphenicol, and chlortetracycline.

Comments

The fact that the correct diagnosis could not be arrived at sooner was largely because the patient had been admitted in a diabetic coma, which was probably also responsible for the extent of the lesion found at operation. A precise history could not be obtained on admission, and perforation of the gangrenous part of the caecum had probably occurred while the patient was comatose. On reviewing the literature on acute phlegmonous caecitis I was unable to find a case that was complicated by diabetes mellitus. Lowered resistance to infection, so commonly found in this disease, was presumably responsible for the extent of the peritonitis.

Two types of phlegmonous caecitis are usually described, and the case reported was of the circumscribed variety progressing later to gangrene and subsequent perforation with general peritonitis. In spite of the very high mortality for cases of advanced acute phlegmonous caecitis (45%), the patient made a remarkable recovery.

Summary

A further case of acute phlegmonous caecitis is described. The condition is still relatively uncommon and a correct diagnosis is almost impossible. Some authors draw attention to the presence of a mass in the right iliac fossa in the early stages, appearing soon after the onset of symptoms. The case reported was complicated by diabetic coma, which added to the difficulties and probably delayed adequate treatment.

The two types of the disease, circumscribed and diffuse, are described and the respective treatment is discussed. In the case reported, exteriorization of the affected part of the caecum, utilizing the gangrenous part of the caecal wall for a caecostomy, was carried out successfully.

I wish to thank Mr. R. S. Ninian, senior surgeon, Maelor General Hospital, Wrexham, for permission to treat and publish this case, and also Dr. J. Forbes, physician, under whose care the patient was originally admitted.

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Medical Memoranda

Dextrocardia, Situs Inversus, and Twinning

A possible relationship between dextrocardia, situs inversus, and twinning has received some attention from geneticists. Thus, Ruud and Spemann (1922) produced situs inversus by division of the amphibian egg, the twin derived from the right half frequently showing this abnormality. This mirror-image mechanism, while a most attractive hypothesis, obviously does not occur in humans, as otherwise the condition would be relatively common. Reports of the incidence of situs inversus vary considerably, LeWald (1925) giving an incidence as low as 1 in 1,400, while Tanner-Cain and Crump (1951) quote an incidence of 1 in 35,000 in the United States Army recruits in 1947. Cockayne (1938) gives a figure of 1 in 19,500, which is probably more accurate, and is in agreement with most figures reported in the literature.

The purpose of this paper is to report an apparent association between dextrocardia, situs inversus, and a family history of twinning in ascendants and collaterals. This occurred in four out of five cases seen in general practice and school medical inspection. The first patient volunteered such a history, and investigation of three other cases, seen over a period of years, tends to confirm this finding.

Case Histories

Case 1.—A man aged 44. On routine examination in general practice in Lancashire a previously unknown situs inversus was diagnosed. This finding was subsequently confirmed by chest *x*-ray examination, screening, and barium meal. The mother and father were each one of twins.

Case 2.—A woman aged 48. Situs inversus was found on routine examination in general practice in Lancashire. The existence of this condition had been diagnosed previously as a result of an abdominal operation. Confirmation was obtained on *x*-ray and barium-meal examination. (*a*) The grandmother and grandfather were each one of twins. (*b*) A sister had twins. (*c*) An uncle had three sets of twins.

Case 3.—A girl aged 7. Previously unknown situs inversus was diagnosed at a routine school medical inspection in Lancashire. There was, in addition, a systolic murmur in the mitral area, suggestive of a small septal defect. This finding was confirmed by *x*-ray examination, screening, and electrocardiogram. It is of interest to record that her brother, aged 11, had a precisely similar systolic murmur in the mitral area, but no transposition of the viscera. (*a*) The father is a twin. (*b*) The paternal grandmother, twice married, had a set of twins by each husband.

Case 4.—A boy aged 6. Dextrocardia without reversal of viscera was diagnosed at a school medical inspection in Roscommon. There was, in addition, cyanosis of the lips and finger-tips, and a moderate degree of clubbing of the fingers and toes. A loud systolic murmur was audible at the base maximal to the right of the sternum, and a systolic thrill was also palpable. Pulmonary stenosis was the probable diagnosis. However, in view of the complicated necropsy findings in previously reported cases of isolated dextrocardia, it is possible that a more complex lesion may have been present. The diagnosis of dextrocardia was confirmed by *x*-ray examination and E.C.G. (*a*) The mother is a twin, probably monozygotic in type. (*b*) A full cousin, resident in America, has two sets of twins.

Case 5.—A girl aged 10. Previously unknown situs inversus was diagnosed at a routine school medical inspection in Lancashire. It was subsequently confirmed by *x*-ray examination and E.C.G. This was an adopted child, and it was not possible to investigate the family history.

Discussion

The exact genetic mechanism of situs inversus is in doubt. An association with twinning is mentioned by Doolittle (1907), who observed dextrocardia in a man who had a twin sister; both of his parents were one of twins, and he produced opposite-sexed twins, the boy showing dextrocardia. Foerster (1861) observed that in the majority of conjoined twins, particularly thoracopagi and pygopagi, one had complete or partial transposition of the viscera, and he advanced the theory that in cases of transposition there has been monozygotic twinning, with the subsequent death and absorption of the normal twin. This finding was not confirmed in the conjoined twins of Kano (Aird, 1954). In this instance there was dextrorotation of the heart in the twin surviving separation, but the E.C.G. was not that of a case of situs inversus. It was concluded, therefore, that there was no true mirror-image of the twins. Aird, however, states that 73% of conjoined twins show the latter abnormality.

In an extensive review of the subject, Cockayne (1938) stated that situs inversus is transmitted as a recessive characteristic caused by a single autosomal gene. He cited as proof for this theory, "its familial incidence and general distribution within a family, its occurrence in both members of a pair of monozygotic twins, and the high percentage of first-cousin marriages that give rise to it. In addition, the ratio of affected to normal sibs in the fraternities agreed with that expected of a recessive character." Twinning has long been admitted by both the medical and the actuarial professions to be a hereditary character, and if this association with twinning is accepted it tends to confirm that theory. However, there is some difficulty in explaining the occurrence of situs inversus discordantly in monozygotic twins. This was first reported by Dubreuil-Chambardel (1927) and has since been reported on a number of occasions, the most recent being that of Helweg-Larson (1947) in a pair of male twins. The normal twin produced one child and a pair of twins that miscarried.

Torgersen (1950) published details of 270 cases of situs inversus, discovered by mass radiography in Norway. He collected data concerning the familial occurrence of twinning in 100 unselected cases. He concluded that it did not

occur in any greater frequency than that expected in a normal population group. In a further investigation of families where the person with situs inversus was a twin, he concluded that the familial incidence of twinning was probably increased in this rare type of case. These findings are in conflict with my admittedly small series. However, the history of twinning in ascendants and collaterals in the families I have investigated is so striking that I suggest that this fact may be of importance genetically in some cases of situs inversus and is not mere coincidence.

I am indebted to Dr. M. L. Thomson, Royal Manchester Children's Hospital, and Dr. S. P. O'Toole, St. Patrick's Chest Hospital, Castlerea, for clinical investigation of Cases 3 and 4.

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A Case of Congenital Extra-abdominal Herniation of Bowel

The usual form of congenital herniation of abdominal viscera is into the base of the umbilical cord and is known as an omphalocele. An omphalocele has a large peritoneal sac which is not covered by skin. In the following case report the criteria necessary for the diagnosis of omphalocele are not present in that (1) the umbilical cord was normal and in no way connected with the hernia, and (2) the bowel had no parietal peritoneal covering. This case is recorded because standard works on the subject bear no description of such a congenital anomaly.

Case Report

An infant was admitted to hospital on December 15, 1954, at the age of ½ hour. She was the first-born infant of parents both aged 28. The pregnancy had been uneventful; following spontaneous rupture of the membranes at thirty-four weeks a normal delivery resulted. Delivery was in a maternity home, and at birth the family practitioner (Dr. Philip Hogg) noticed the herniation of bowel and brought the infant immediately into hospital.

Examination revealed a newborn female baby in good general condition, although there was slight cyanosis of the lips. She cried lustily and was quite active. Her birth weight was estimated at 5 lb. (2.3 kg.). Physical examination revealed nothing abnormal apart from a cleft soft palate and the defect being described. The umbilical cord was normal, but 1 in. (2.5 cm.) to the right of the umbilicus, and separated by normal skin, was a clean-cut defect of the abdominal wall looking like a stab wound, through which approximately 2 ft. (60 cm.) of small bowel protruded (see illustration). There was no parietal peritoneal covering over the bowel and no hernial sac was present. The visceral peritoneum was thickened and the gut was brownish black in colour. Clinically there was doubt concerning the viability of the affected gut.

Operation.—At operation, by Mr. Stewart Feggetter two hours later, the 2 ft. (60 cm.) of thickened small gut was cleaned with saline and returned to the abdomen after the abdominal wall defect had been enlarged. The umbilical stump was removed and the abdomen closed in two layers.

Because of the excellence of the baby's general condition intravenous therapy was not given pre-operatively, and for the next few days she gave no cause for alarm. Intramuscular penicillin, 50,000 units six-hourly, and streptomycin, 50 mg. twice daily, were started immediately after operation because of the possibility of peritonitis developing. Gastric suction during the next three days produced minimal quantities of bile-stained fluid, and as she had had three small bowel actions by December 18 oral feeding was then begun for the first time. Hourly feeds of 1 dr. (3.5 ml.) of glucose-saline were given initially, and when this was taken reasonably well the amount was increased and she was changed over to half-cream national dried milk.

On December 24 vomiting started and her abdomen was seen to be distended. She had passed only one small motion in five days, and as a radiograph of the abdomen revealed the presence of fluid levels it was presumed that there was an obstruction. She was treated medically with intravenous fluids and gastric suction, and by December 26 the distension had disappeared and once more oral feeding was begun. From December 27 to 30 bowel washouts were

Drawing of the case, showing protrusion of small bowel.

given daily and normal results obtained, but on December 29 once again abdominal distension was noticed, but no vomiting occurred. The distension disappeared after her daily washout.

On January 1, 1955, she had her first spontaneous motion, and, as from then onwards she had spontaneous normal motions each day, the bowel washouts were discontinued. Her weight, which was 4 lb. 11 oz. (2.1 kg.) on December 19 and remained more or less stationary until January 1, started to increase, and on January 12 she was discharged weighing 5 lb. 11 oz. (2.6 kg.) and feeding satisfactorily.

On January 21 her mother reported that the infant had given "no trouble." Her weight had increased to 6 lb. 1½ oz. (2.8 kg.) in the nine days, and examination showed her to be a lusty normal baby. On February 22 her weight had risen to 8 lb. 15½ oz. (4.07 kg.). She was in excellent general condition, but a small ventral hernia was present at the lower end of her abdominal wound. When last seen, on March 22 at the age of 14 weeks, she weighed 11 lb. (5 kg.).

Comment

This form of hernia must be extremely rare, and, in view of the stab-like wound through which the gut protruded, one might consider the hernia to be traumatic in origin. However, the appearance of the gut suggested that it had been outside the abdominal cavity for a long time during intrauterine life. This suggested that its origin was congenital. Congenital abnormalities are often multiple, and the presence of a cleft soft palate seems to be further evidence in favour of its congenital origin.

With such a lesion, peritonitis and/or intestinal obstruction from adhesions is always a possible complication. Apart from the episode described above, this has not presented a problem to date, although it is possible that intestinal obstruction may develop in the future.

I thank Dr. Philip Hogg for the speed with which he brought the infant into our care, and Dr. George Davison and Mr. Stewart Feggetter for allowing me to publish this case history. I am extremely grateful to Dr. Davison for his helpful criticism.

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Reviews

UROLOGY

Urology. Volumes I, II, and III. Edited by Meredith Campbell, M.S., M.D., F.A.C.S. With the collaboration of fifty-one contributing authors. (Volume I: Pp. 1–862; Volume II: Pp. 863–1666; Volume III: Pp. 1667–2356. 1,148 illustrations. £15.) Philadelphia and London: W. B. Saunders Company. 1954.

The growth of interest in urology is world-wide and the resulting literature is vast. With one or two notable exceptions books on the subject have been the work of individuals, but the editor of this comprehensive treatise has recognized the need for enlisting a team of experts to cover the subject adequately. Although this must inevitably lead to some variations in literary style, and even some inconsistencies, the individual contributions are so authoritative and the editorial discipline has been so good that the whole work forms an unrivalled account of present-day opinions on the subject. The more complete separation of urology from general surgery in America than in Great Britain has led to greater specialization within the subject, and this is reflected in the editor's choice of contributors, each of whom is a recognized authority in the matter on which he writes.

There are three volumes each of about 800 pages. The first includes the relevant anatomy, physiology, and embryology, together with diagnostic methods, the pathology of obstruction, infections, infertility, and stone. In the second are found the accounts of injuries, tumours, neuromuscular disease, urology in women, and an important section on urology in infancy and childhood written by the editor himself and giving in effect a summary of his major work on the same subject. The third volume is occupied mainly by surgical methods, but includes sections on radiotherapy, medical diseases, and endocrinology.

It is difficult to choose from this wealth of material sections for particular comment without appearing to do injustice to others, and the choice must perforce be dictated to some extent by personal interests. Jewett, writing on tumours of the bladder, emphasizes the overwhelming importance of infiltration of the bladder muscle as an index of prognosis, and exposes the limits of total cystectomy in the treatment of bladder cancer. In his chapter on tumours of the kidney Deming gives a very complete classification. I doubt the advantage of separating "hypernephroma" from adenocarcinoma; in the former removal of glands about the renal pedicle is described as futile, whereas in the latter it is advised. Even if a pathological difference does exist a pre-operative clinical distinction between the two is virtually impossible. Nor is the prognostic importance of the histological grade of the tumour and the presence of venous involvement emphasized as it deserves. Neither he nor Priestley, who writes on the surgery of the kidney, appear to be greatly in favour of the transthoracic route for nephrectomy, a matter in which I am in agreement. Creevy's chapter on pre-operative and post-operative care is remarkable for its sound common sense; his statement that "the knowledge that the patient can pitch hay all afternoon or can run upstairs is worth more than a medical consultation in proving that the cardiac function is adequate" should be drilled into all urologists; so also should his advice not to try and "prepare" the urinary tract of the prostatic who is a good risk. As well as these simple home truths he gives an intelligible account of water and electrolyte balance.

There are many attractive features about these well-produced volumes which deserve mention, not the least of them being the repetition of the index to the whole work in each volume. Most of the references are naturally from the American literature, but the British are not completely neglected, especially in the chapter on renal injuries. A few sections, however, are completely devoid of references, and this is one of the minor inconsistencies of the multiple author work.

Dr. Campbell's dedication, "To those who may be helped by these volumes," is likely to be applicable to the vast majority of urologists throughout the world.

E. W. Riches.

MEDICAL STATISTICS

Principles of Medical Statistics. By A. Bradford Hill, C.B.E., D.Sc., Ph.D., F.R.S. 6th ed. (Pp. 314+ix; 10s. 6d.) London: The Lancet Ltd. 1955.

In the 18 years between the appearance of the first and sixth editions of this popular guide-book to medical statistics the climate of opinion has undergone changes, some of which—despite the author's warnings against deducing causation from a mere correspondence in time trends—may be regarded as evidence of the success of the work itself. Application of statistical method to medical research, particularly in connexion with the effectiveness of treatment, may still be considered a dull pastime, but it is no longer regarded as unnecessary. Indeed, the pendulum has been swinging so far as to elevate the χ^2 test to a kind of charm whose presence in a medical paper is a guarantee that the conclusions are beyond question. There are signs that this phase of exaggerated confidence in "statistical significance"—which so often follows the introduction of tests which are easy of application—is giving place to a better understanding of what such tests can do and what they cannot do. On rereading this handbook one is struck by the author's reiterated warnings that differences cannot be regarded as significant unless proper care has first been taken to ensure that the data being compared are in fact comparable.

Useful additions to the sixth edition are a chapter on clinical trials, which is full of sound advice, and a table of random sample numbers for use in such trials as well as for other purposes. The clarity and simplicity of exposition continue to be admirable features of the book.

Percy Stocks.

SYNOPSIS OF MICROBIOLOGY

Review of Medical Microbiology. By Ernest Jawetz, Ph.D., M.D., Joseph L. Melnick, Ph.D., and Edward A. Adelberg, Ph.D. (Pp. 360; illustrated. $4.50.) Los Altos, California: Lange Medical Publications. 1954.

This volume is the ninth of a series described as "a concise medical library for practitioner and student." Although revision is promised biennially, it is not a review of recent developments but a synopsis of the entire subject, printed in small type by the lithographic process, and hence reasonably priced although a work of some magnitude. The introductory chapters on bacterial morphology, metabolism, and variation are admirable, and include accounts of such novel phenomena as recombination, transformation, and transduction. Other general subjects dealt with are classification, chemotherapy, and immunology. In the systematic section which follows, bacteria and the infections caused by them occupy only 70 pages and viruses 100, a disproportion not wholly accounted for by the great expansion in knowledge of virology but due in part to more comprehensive treatment of this subject. There are also chapters on fungi and on bacteriophage, the latter clearly describing studies which have revealed the minutiae of phage behaviour, and defining many new terms which have come into use in this connexion. On the other hand, there is no mention of phage typing, either here or in the sections on the salmonellas and staphylococci, nor in the rather confused description of streptococci is there any suggestion that serological typing of *Str. pyogenes* has been of value in epidemiological studies. How to regard such omissions depends on the type of user for whom the book is primarily intended. The readers served best are those seeking succinct information about the more abstruse theoretical aspects of the subject, and the practising physician wanting information about available diagnostic tests for almost any conceivable infection, especially if due to a virus. The illustrations vary from line drawings, some so crude as to be barely recognizable, to excellent electron micrographs, of which there are many. The mass of information provided is very up to date and almost uniformly

accurate, but Vincent's angina is not, as stated on p. 202, the same thing as "trench mouth," and the fact that *Actinomyces bovis* and *A. israeli* have been distinguished as separate species by serological and other methods has escaped the authors' attention.

Few people will envy the authors' task of revising this ambitious text at set and frequent intervals, but if they do so it should remain a very helpful work of reference.

L. P. GARROD.

HEART DISEASE IN INFANCY

Herzkrankheiten im Säuglingsalter. By Dr. Ettore Rossi. Foreword by Professor Dr. Guido Fanconi. (Pp. 373+xiii; illustrated. D.M. 65.) Stuttgart: Georg Thieme. 1954.

This book on heart disease in infancy covers an important aspect of cardiology very well. To begin with there is a chapter on the normal features of the heart at this age. The table of the cardiographic "normals" is full, clear, and useful. Then comes a long chapter on congenital defects. Lesions of the aortic valves and of the aorta are grouped together. Under transposition of the great vessels are many abnormalities, including, of course, those associated with the names of Fallot, Eisenmenger, and others. This is very well done. The difficult subject of transposition is made much clearer by this approach, and convictions which at first sight look like isolated and unrelated abnormalities are joined by a feature common to them all. There are some excellent diagrams. Another section deals with defects of the cardiac septa, and other isolated lesions come in here. It is odd that uncomplicated pulmonary stenosis is not mentioned at all; nor are some of the abnormalities of the aortic arch. The third section deals with myocarditis and, still more important, myocardosis. Here is provided much valuable information. The results of congenital lesions of the coronary arteries are again dealt with. Enlargement of the heart is the outstanding point in all these matters, and it forms the basis for the discussion of various exocardial diseases such as avitaminosis.

The references are very full, and, best of all, the titles of the papers are given. The illustrations throughout are good; naturally skiagrams are affected by the difficulties inevitable in the very young. The cardiograms are only fairly good, for the same reason. There is much useful information in this book, well expressed and illustrated, not easily found elsewhere.

TERENCE EAST.

PAYING FOR MEDICAL CARE

Financing Hospital Care in the United States. Reports of the Commission on Financing of Hospital Care. Volume II, *Prepayment and the Community.* Edited by Harry Becker. (Pp. 356+xxiii. 34s.) Volume III, *Financing Hospital Care for Non-wage and Low-income Groups.* Edited by Harry Becker. (Pp. 110+xvii. 19s.) New York, Toronto, London: McGraw-Hill Book Company. 1955.

Paying for Medical Care in the United States. By Oscar N. Serbein, jr. (Pp. 543+xxiv. $7.) New York: Columbia University Press. 1953.

In Britain the rising cost of medical care—and how to pay for it—brings uneasy nights to Her Majesty's Government rather than to the individual citizen. The citizen is certainly affected as a taxpayer, but he tends to overlook this fraction of the very large bill for the public services for which the money is extracted from him by methods too well known and too painful to warrant recapitulation. But the not inconsiderable number who desire, and are prepared to pay for, private treatment, as well as the doctors who provide it, do have an interest in how our cousins across the water are tackling the problem of meeting hospital and doctors' bills. These books supply the information.

The Commission on Financing of Hospital Care has 36 members, is non-governmental, was financed by several of the educational and research trusts, and charged itself with the task of studying "the costs of providing adequate hospital services" and determining "the best systems of payment for such services." The two volumes it has now published are a mine of information. In the U.S.A. there are 419,871 beds in 4,518 non-profitmaking and "proprietary" hospitals. The index cost of maintaining them in 1951 was 260, the base line of 100 being the average cost in 1935–9. During the same period the general cost-of-living index rose to 185.6.

The solution of the problem of maintaining the solvency of the hospitals recommended by the commission, two members dissenting, is by an even greater extension of prepayment schemes. There has been a great drive for membership by "Blue Cross" and by commercial insurers: 59% of the population is now covered compared with 9.3% in 1940. But few of the schemes give complete cover; the premiums are not small; and large groups, such as the aged, the indigent, the disabled, those with chronic illness, the unemployed, and the employed with low incomes cannot afford them. The majority of the commission suggest various means by which public funds, administered locally, should pay for the hospital treatment of these groups in voluntary hospitals, but this involves a means test to which the two who sign minority reports object.

Dr. Serbein, who is assistant professor of statistics at the Graduate School of Business, Columbia University, covers a larger field of inquiry, and deals not only with hospitals but with prepayment schemes for all forms of medical, and even dental, care. He includes the "Blue Shield" scheme for meeting the charges made by doctors for hospital treatment, and group practice prepayment plans for domiciliary treatment and health supervision. He describes all the health services of the U.S.A. in considerable detail.

All three books are well written, well documented, and well indexed.

ALLEN DALEY.

WAR EXPERIENCES OF A SURGEON

Surgeon at War. By Lieutenant-Colonel J. C. Watts, *M.C.*, F.R.C.S., R.A.M.C. (Pp. 165; illustrated. 12s. 6d.) London: George Allen and Unwin Ltd. 1955.

In 1937 Philip Mitchiner advised one of his house-surgeons at St. Thomas's (who was also staff-sergeant in the O.T.C.) to join the Royal Army Medical Corps, for, said he, "there is going to be a war within three years, so you might as well be in at the start." The youth followed his chief's advice, had a remarkable time on active service in many countries, and now, as Lieutenant-Colonel J. C. Watts, has written an interesting account of his wartime experiences. Such personal histories are most useful supplements to the more impersonal official histories.

The author saw service in Palestine, the Western Desert, Egypt, Syria, Italy, in Normandy on D Day, in Germany at the crossing of the Rhine, and finally in Singapore, Java, and Korea—surely a record hard to beat. As surgical specialist he was also fortunate to obtain excellent practical experience and to do a fine job of professional work.

He writes with an easy, matter-of-fact style, but occasionally his plain account is the more vivid because of its simplicity. For part of the time he was with an airborne unit, and thus describes the scene after the landing: "The landing zone looked rather like a fairground in process of closing down, the discarded parachutes resembling struck tents, and all the litter of war lying around. Only the still figures of the dead gave an air of grim reality to the scene."

The author is a sportsman and has a sense of humour, and in the intervals of more serious activities had ample opportunities to exercise his talents in these directions. On one occasion he impersonated an Arab sheik and another time a German officer, and quiet times were filled in with sailing, skiing, and swimming. In Korea he was for a time in an Australian mess, and comments: "The Australian system of rationing was very simple, consisting of a meat meal every two hours, and tea and sandwiches in between, in case you felt faint." In Indonesia the author was once addressed as "Mr. Dr. Colonel Watts Esq."

From the purely surgical point of view the book contains little that is new, and there is much explanation of elementary medical facts, intended, presumably, for the laity. The book is of value, however, as a personal contribution to the history of the war.

ZACHARY COPE.

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LUNG CANCER AND POLLUTED AIR

The evidence that smog can produce acute illness and even death is unequivocal, but whether continued exposure to a lesser degree of pollution can be a cause of chronic illness is uncertain. From a study of local differences in the death rate from lung cancer Dr. Percy Stocks[1] suggested in 1947 that "either smokiness of the atmosphere is an important factor in itself in producing cancer of the lung, or sunshine is an important factor in preventing its incidence." Other studies from Britain,[2 3] Denmark,[4] Finland,[5] Norway,[6] and the U.S.A.[7] have consistently shown that the recorded mortality is higher in urban than in rural areas. The differences have not been great, but whenever more detailed data have been available the mortality is seen to be systematically related to the degree of urbanization. The hypothesis that pollution of town air is a cause of these differences has been strengthened by the recognition of three carcinogens—arsenic, 3:4-benzpyrene, and radium—in the smoke from chimneys or the fumes from cars.

There are, however, difficulties in accepting the hypothesis. It is impossible, for instance, to correlate the great increase in the mortality from lung cancer with the change in smoke production, and there is evidence that men who have had special occupational exposure to motor fumes have not had an abnormally high mortality from the disease.[8] Alternative explanations of the urban–rural differences have therefore been sought, and L. Kreyberg[9] has concluded that in Norway the urban excess was probably due to differences in the personal habits of townsmen and countrymen. One relevant difference is a difference in smoking habits. Several workers[10 11] have found that townsmen smoke more than countrymen, and that, of townsmen who smoke, a higher proportion smoke cigarettes. Since it has been established that there is a causal connexion between cigarette-smoking and lung cancer, it is clearly necessary to take these differences in smoking habits into account when comparing mortality rates in different areas. Few studies have hitherto been on a large enough scale to allow this to be attempted, so that the results of the extensive investigation initiated in 1952 by the Cheshire and North Wales Branch of the British Empire Cancer Campaign have been awaited with considerable interest. The report now presented by Dr. Percy Stocks and Dr. John M. Campbell in our opening pages this week is, as they stress, an interim one, and the conclusions may need to be modified in the final analysis. They have presented it now, without waiting for the completion of the five years which the investigation is planned to cover, because the data already obtained "seem to point strongly to certain conclusions which might conceivably help to hasten effective action towards reducing lung cancer incidence."

Since 1952 a collection has been made of the past environmental histories of residents in North Wales and the Liverpool Hospital Region who were diagnosed as suffering from any form of malignant disease. Notifications have also been obtained of all deaths certified as due to cancer, and, if no history had been taken from the patient during life, the history has been sought from a relative through the agency of the local medical officer of health and his health visitors. The history, which is standardized, covers many aspects of the social environment and includes the patient's smoking history throughout the whole of his life. From early in 1953 the same questions have been asked of adult patients admitted to a Liverpool hospital and to the hospitals at Chester, Wrexham, Bangor, and Llandudno. Some 12,000 histories have been obtained in this way from patients without cancer. From the data given in these histories and from population data given by the census, estimates have been made of the numbers of persons resident in different parts of the region who smoke different quantities of tobacco. Estimates of the corresponding numbers of persons dying with lung cancer have been made from the data given by the histories of the cancer patients; and an estimate of the lung cancer mortality in different areas at different levels of smoking has been made by comparing the two sets of data. The present paper is limited to consideration of the mortality among men aged 45 to 74 years. In this age group Stocks and Campbell estimate that the annual male mortality from lung cancer in the rural areas of Anglesey and Caernarvon increases steadily from 14 per 100,000 for non-smokers to 363 per 100,000 for heavy smokers (defined as men who have averaged more than 250 cigarettes a week for any period of 10 years). The

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[2] Curwen, M. P., Kennaway, E. L., and Kennaway, N. M., *Brit. J. Cancer*, 1954, **8**, 181.
[3] McKinlay, P., *Hlth Bull. (Edinb.)*, 1953, **11**, 1.
[4] Clemmesen, J., Nielsen, A., and Jensen, E., *Acta Un. int. Cancr.*, 1953, **9**, 603.
[5] Saxen, E. To be published.
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[7] Hoffman, E. F., and Gilliam, A. C., *Publ. Hlth Rep. (Wash.)*, 1954, **69**, 1033.
[8] Doll, R., *British Medical Journal*, 1953, **2**, 521 and 585.
[9] Kreyberg, L., *Brit. J. Cancer*, 1954, **8**, 605.
[10] Doll, R., and Hill, A. B., *British Medical Journal*, 1952, **2**, 1271.
[11] Hammond, E. C., and Horn, D., *J. Amer. med. Ass.*, 1954, **154**, 1316.
[12] Doll, R., *Brit. J. Cancer*, 1953, **7**, 303.
[13] Hammond, E. C., and Horn, D. Paper read at annual meeting of American Medical Association, 1955.

corresponding mortality for pipe smokers, irrespective of quantity, was 41 per 100,000. Rates of about the same magnitude are found for the mixed urban and rural areas centred on Chester and Wrexham, but in Liverpool the estimated rate in non-smokers is much higher (131 per 100,000) and the increase in smokers (up to 394 per 100,000) is relatively less. From these figures Stocks and Campbell deduce that the abolition of cigarette-smoking might be expected eventually to reduce the deaths from lung cancer of men in Liverpool by about one-half, and that three-eighths of the deaths are due to some local cause only slightly present in the rural areas. In rural areas, on the other hand, the great majority of cases might be eliminated by the abolition of smoking alone.

The extent of the atmospheric pollution in the three areas was measured at five stations during the winter of 1954. At Liverpool the amount of smoke was found to be six times greater than in the rural areas, the amounts of sulphur dioxide and 1:12-benzperylene eight times greater, and the amount of 3:4-benzpyrene 10 times greater. Hence, if a "standard" man breathes outdoor air all the time and all the benzpyrene content reaches the lungs, the average annual intake would be about 41 μg. in the rural areas and about 450 μg. in Liverpool. The amount actually inspired is likely to be less than these maximum figures, and Stocks and Campbell find that, if they add between one-quarter and one-twelfth of them to the amounts estimated to be derived from cigarette smoking, the relative value of the combined intake of benzpyrene in town and country is closely proportional to the ratio of death rates at each level of cigarette consumption. They therefore suggest that benzpyrene may be the agent responsible for the association of lung cancer with both smoking and urban residence.

The case is closely argued, and the authors' claim that their hypothesis "now appears to be tenable" will be readily admitted. To regard it as established, however, would be to neglect their own proper caution in drawing conclusions. The only two other investigations which have attempted to take smoking histories into account in comparing regional differences in lung cancer mortality have led to the conclusion that a specifically urban factor is not likely to be important.[12 13] In the present investigation elements of doubt mainly derive from the interval of time between the collection of the data and the period when the carcinogens must be presumed to have been most effective, and the difference in the methods used to collect information from the patients with or without cancer. Memory of tobacco consumption 30 or 40 years previously is, even with the patient, very uncertain, and a widow need not necessarily ever have been aware of the amount consumed—or indeed whether a non-smoking husband ever was a smoker. In 35 cases information was procured from both the patient and his widow, and this suggests that the widow's estimate was apt to be low. As the investigation progresses, more such cases will occur, and the size of the error and of the necessary correcting factor can be calculated with greater confidence. It may then also be possible to make estimates of the cancer mortality, with the use only of data derived directly from the living patient, and to seek corroboration from the estimated death rate in women.

WORLD MEDICAL ASSOCIATION

The twenty-fourth session of the council of the World Medical Association and the ninth General Assembly were held in Vienna last month. Their deliberations and decisions showed beyond doubt the essential role now assumed by the W.M.A. at the international level in medical affairs. The principal activities of the W.M.A. have been in the fields of medical ethics, international medical law, medical education, and social security. As each year has succeeded another since its establishment in 1947 the W.M.A. has found itself obliged to tackle a number of other matters of importance to the professional life of the doctor and so to the national associations that constitute the membership of the W.M.A., now collectively representing some 700,000 medical men and women in more than 50 countries. It is not easy for the individual doctor in India, England, or Yugoslavia to see what there is in the work of the W.M.A. that will benefit him—as an individual. Such an attitude is understandable, and is, indeed, often unreflectingly adopted by the individual member in relation to his own national medical association. But we live at a time when men, uncomfortably conscious of the unity of the world in which they exist, come together in international assemblies to discuss common problems with a view to taking common decisions that are bound to have an impact on the lives of individuals.

The United Nations has set the pattern at inter-governmental level, and of its specialized agencies the World Health Organization and the International Labour Organization are a powerful force in the development of medicine, backed as they are by government authority and money. In this setting there is only one body which can act as the watch-dog for the national medical associations and so for the individual practising doctor—and that is the World Medical Association. This it does on a budget and a secretarial staff that are Lilliputian in comparison with, for example, those of the World

Health Organization. But through the untiring efforts of the secretary-general of the W.M.A., Dr. Louis H. Bauer, and his staff in New York, and the generous financial assistance coming from the United States, the W.M.A. has made its influence felt and increasingly felt. Money provided by the subscriptions of national medical associations goes only a small way towards meeting the costs of the W.M.A.: but this, too, grows in volume, and it may be hoped that in time the member associations of the W.M.A. will in fact wholly support by their contributions the work of an organization which is indispensable to the maintenance of professional ideals and interests in an age when the encroachment of government on medicine is one of the inescapable facts of the modern world. It is, for example, of interest to note that in the recent conflict in which the Austrian medical profession was engaged its leaders took their stand, and secured part of their claims, on the basis of the twelve principles of social security laid down by the World Medical Association.

The working out of the relations between medicine and society is the outstanding professional problem of the day, and the debate in the General Assembly at Vienna last month on social security bore witness to this. In opening this debate Dr. Dag Knutson, who has just completed his term of office as chairman of the W.M.A. Council, observed that in principle doctors are not opposed to the idea of social security, but find much to disagree with in the ways it is being developed—in particular the dangers of bureaucracy and top-heavy administrative machinery. "They tend," he said, "to come between the doctor and his patient, transforming the latter from an individual needing health care to a social mass demanding benefits"; doctors, he added, "refuse to be looked upon as technicians in the service of institutions." Dr. Knutson pointed out that a very large part of the costs of social security "goes through the hands of the medical profession," this in itself adding to their obligations. Those responsible for administering social security, for providing the money to cover the costs of medical care, tend to look on the doctor as an employee whose actions must come under their control, and so an inevitable conflict arises. In the Lima Medical Declaration[1] of 1949, for example, it was recommended that an attempt should be made to "evaluate the work of the doctor on the basis of efficiency, rapidity, and economy of the diagnosis and treatment of the cases and not merely be based on the number of consultations, operations and medical acts performed." As the administrators of social security schemes are not able to assess the "efficiency" of medical acts, they are likely to concentrate their attention on "rapidity" and on "economy." At Vienna last month the social security committee of the W.M.A. spent two long days in a discussion of such matters with representatives of the International Social Security Association, an influential body closely linked to the International Labour Organization. Those discussions are to continue, and represent a highly significant move to clear away misunderstandings and to approach, if possible, some measure of agreement. As Dr. Knutson said in concluding his address to the General Assembly, "The medical profession must state that medicine, an age-old art merged with a young science, should set its own conditions of practice, with social security systems assisting in the achievement of the ultimate goal."

However different may be the methods of providing medical care in different countries, certain principles and ideals of medicine are, or should be, inalienable. What happens in one country has its effect on what happens in others, and for this reason alone the World Medical Association needs and deserves the active interest and support of its national member associations and of their individual members. Britain has much to offer in experience; it also can learn much from the experience of other countries. If we emphasize here one aspect of the work of the W.M.A. it is because this grows in significance year by year, and the outcome of it all will profoundly affect the professional life of the practising doctor no matter where he lives.

[1] *Arch. Col. méd. Salvador*, 1949, **2**, 211.

DIABETES MELLITUS IN INFANCY

The excitement in recording the youngest patient to suffer from a disease is rather like that of recording the earliest cuckoo of the year, and by itself it is of about as much value. But reports of this character, as they accumulate, may increase our knowledge of the nature of the disease and show what effect the immaturity of the victim has on the symptomatology, treatment, and prognosis. Two such case histories of diabetes in infancy have recently appeared.[1,2] In the first Mary Wylie described an infant who probably had diabetes from birth. The condition was controlled by insulin, and the infant made good progress and is still having insulin. In the second S. Keidan described a case with a somewhat similar initial history, but with the disease starting at 3 weeks of age; the subsequent progress was entirely different. This infant did not need insulin and appears to have made a complete spontaneous recovery. Keidan has found descriptions of five other cases of transient "diabetes" in the main resembling his own. He also has collected the records of infantile

[1] Wylie, M. E. S., *Arch. Dis. Childh.*, 1953, **28**, 297.
[2] Keidan, S. E., ibid., 1955, **30**, 291.
[3] Himsworth, H. P., *Lancet*, 1936, **1**, 127.
[4] Lawrence, R. D., *British Medical Journal*, 1951, **1**, 373.
[5] Nelson, W. E., *Textbook of Paediatrics*, 6th ed., 1954, p. 1275. Philadelphia.
[6] Guest, G. M., *Amer. J. Dis. Child.*, 1948, **75**, 461.

diabetes and discusses the age distribution in the first twelve months of life. From this it appears that in the first three months more cases of "diabetes" are recorded than in the following six months; after this the incidence of diabetes again increases.

Diabetes in the young is a clear-cut disease with an acute onset and with a steadily increasing need for insulin as the years pass. In most cases, however, after the initial hyperglycaemia is overcome by insulin there is a period of remission when much less insulin is needed. Occasionally the insulin may be completely omitted, but within a year at the longest it is again required and must be maintained thereafter. Exceptions to this rule are so rare that the validity of the diagnosis in such cases of protracted remission has to be carefully considered. There is indeed no absolute definition of diabetes, for the cause may vary in different cases; two main types of diabetes[3,4] have often been postulated.

In early infancy hyperglycaemia may be found in many acute infections[5] and also occasionally in diseases affecting the central nervous system. This hyperglycaemia is short-lived. Whether it produces any symptoms cannot be easily determined, for usually the effects of the causative condition overshadow it. It is difficult to exclude some such acute disease in many of the neonatal cases described as transient diabetes. Keidan's patient, although the hyperglycaemia was without apparent cause, had several generalized convulsions and an abnormal cerebrospinal fluid. But perhaps in the neonatal period the condition is reversible and the transient remission found in the older child is permanent in the newborn. Although it rather begs the question, one answer to the problem is to assume that the insulin-sensitive type of diabetes is always permanent, and that if a cure occurs it was not diabetes.

The other kind of information to be obtained from these records of cases in young people is on how symptoms and treatment are modified by the immaturity of the subject. Of the triad of symptoms of acute diabetes—thirst, polyuria, and wasting—thirst and polyuria are difficult to detect in an infant, and they were frequently not recorded. Wasting with dehydration was found in all. In some vomiting was also present and suggested a possible, but incorrect, cause for the symptoms. Glycosuria when looked for was always found, but ketosis was often slight. The blood sugar level when estimated was invariably very high, and this finding would exclude such causes of wasting and thirst with glycosuria as the Fanconi–de-Toni–Debré syndrome. The only other condition which could cause all these signs and symptoms is galactosuria, and here hepatomegaly and jaundice usually are present, and more sensitive tests show the sugar present in blood and urine to be galactose and not glucose.

Treatment with insulin is essential and presents a nice problem in management. The inability of the infant to break his diet and the relative constancy of his environment at first sight should make the task simple, but extreme sensitivity to soluble insulin often offsets these factors. Delayed-action insulins have been found helpful in overcoming this difficulty.[6] The prognosis appears to depend on skilled management, and good progress has been reported in those who survived the early hazards of delay in diagnosis and the institution of insulin therapy.

PELVIC ARTERIOGRAPHY

In recent years an increasing number of articles have drawn attention to the value of arteriography of the pelvic vessels in gynaecological and obstetrical diagnosis. A series of valuable contributions on this subject from the Department of Roentgen Diagnosis of the Karolinska Hospital, Stockholm, began in 1952. Four hundred and fifty patients on whom pelvic arteriography was performed during the years 1949–54 form the basis of the latest contribution, an excellent monograph by Ingmar Fernström.[1] The study was planned to determine the arteriographic findings in cases of uterine fibroids, adnexal tumours, and pregnancy (both uterine and ectopic), and from them to assess the diagnostic value of the new techniques. The experience gained in this considerable study has been beautifully presented in the monograph, which also contains a survey of the literature, a description of technique and the complications encountered, which were not serious, as well as an impartial statement on the diagnostic value of the new methods.

Percutaneous puncture of the femoral artery as described by U. Borell *et al.*[2] was found to outline only the ipsilateral uterine vessel in most cases. It was therefore replaced by the insertion of 19 cm. of polythene catheter to reach the bifurcation of the aorta.[3] After applying bilateral femoral artery compression by tourniquets, 40–50 ml. of a 50% solution of "umbradil" was injected in 2–3 seconds through the catheter. Rapid injection was necessary to outline the small pelvic vessels. The catheter was left in position until the films were inspected to allow a second injection if necessary. Renal elimination of the opaque medium being rapid, it was found essential to empty the bladder before repeating the injection and taking a second set of films. Arteriography proved particularly useful in the differential diagnosis of fibroids and adnexal tumours. It was also of value when no tumour could be palpated, as in early unruptured extrauterine pregnancy. A study of the many beautiful plates and drawings illustrating the monograph makes it clear that diagnostic accuracy requires considerable experience both in taking suitable films and in interpreting them. The clinical contribution pelvic arteriography can make appears to be limited. At the fourteenth British Congress of Obstetrics and Gynaecology recently held at Oxford the application of the new techniques to the study of malignant pelvic disease was discussed by H. L. Kottmeier, of Radiumhemmet, Stockholm. The relation to the iliac vessels of masses on the lateral pelvic walls could be determined in this way. Kottmeier's paper, which will be published later this year in the transactions of the congress (*J. Obstet. Gynaec. Brit. Emp.*), introduces a new and possibly valuable diagnostic procedure to all responsible for the treatment of advanced malignant pelvic disease.

[1] Fernström, I., *Acta radiol.* (*Stockh.*), 1955, suppl. 122.
[2] Borell, U., Fernström, I., Lindblom, K., and Westman, A., ibid., 1952, **38**, 247.
[3] Seldinger, S. I., ibid., 1953, **39**, 368.

DIET AND LONGEVITY

Temperance in eating and drinking was accepted as a cause of longevity in early Chinese writings, and even to-day centenarians often ascribe their long lives, almost certainly incorrectly, to particular articles of diet. Metchnikoff,[1] who devoted considerable thought to the prolongation of life, stressed the multiplicity of factors determining life's span. The duration of life is determined by the interaction of heredity and environment, which both influence the rates of growth, development, ageing, and senescence, and which bring on death through disease and accident, or in rare cases cause life to end in "physiological" death. Changes in environment may prolong life, but may also increase its hazards and so cause premature death.

The effect of diet on the life span has been reviewed by M. and Ruth Silberberg.[2] Although many animal studies have been made on the subject, our knowledge of the effect of diet on human longevity is confined largely to impressions and indirectly to life insurance statistics, which show that the obese are not good risks. Fat must come from food, from an excess of intake of calories over expenditure; there is no other source. Insurance figures show that as body weight goes up the expectation of life goes down. Data derived from animals are not always clear cut, and species differ considerably. In a variety of lower animals life may be prolonged by restriction of food, but this is associated with a far-reaching reduction of body size or of vital activities, or of both, to which these species can adjust themselves. The higher species, however, with their complex organization, are less adaptable to drastic food reduction than lower forms of life, particularly during the growing period.

There can be little doubt that moderate dietary restriction during certain periods of life can prolong the life span in some species. For example, in rats of the Sprague-Dawley strain underfeeding increases the rate of survival compared with that of rats fed high carbohydrate diets *ad libitum*, and with rats of the Wistar strain a day without food every three or four days likewise increases longevity.[3] This restricted feeding is effective in prolonging life only if applied after the period of growth. Thus mice adequately fed early in life and subsequently given restricted diets live on the average longer than mice restricted during growth and allowed to feed *ad libitum* later in life. Severe underfeeding just after weaning is incompatible with normal growth and development and may result in increased mortality early in life. The exact age of animals at which restriction of food produces an optimal effect on survival has yet to be determined. In mammals this date may coincide with the stage of development of the long bones, when regressive changes begin to overcome the growth of the epiphysial cartilage.

The effect of various types of food on the life span of animals has been investigated. A high proportion of protein or carbohydrate in the diet does not shorten the life span of the rat, although it is claimed that rats of both sexes live longest if the food contains 14% protein.[4] On the other hand, a high level of fat in the diet, particularly if it contains much cholesterol, has an adverse effect on the life span of some strains of mice and rats.[5,6] The effects are in some respects the opposite to underfeeding, and like the latter differ in degree, depending on strain and sex, duration of test, and the age of the animal at the time of the test. It has been thought that so long as growth, which is a characteristic of youth, is maintained the ageing process can be deferred. The possibility that the administration of exogenous nucleic acid might maintain a high nucleocytoplasmic ratio, typical of youthful tissues, has caused some investigators to test the effect of nucleic acid supplements on the duration of life. In white mice the life span can be prolonged by administering the nuclei of thymic cells and nucleic acid.

Apparently somewhere between the extremes of undernourishment and dietary enrichment lie those regimens that are optimal for longevity. Ideally, these should permit a good and uniform, but not necessarily a fast, rate of growth and development early in life, and should, in order to avoid the injurious effects of overnutrition, subsequently stay at a low level that is yet adequate to permit the animal to live a long but at the same time an active and useful life. How far these observations can be applied to man we do not know. Controlled feeding tests on human beings on a scale capable of statistical analysis are impossible. Life insurance figures show that the slim outlive the obese, and some evidence suggests that a high fat intake predisposes to cardiovascular disease in man. There is therefore much to be said for restricting food intake, particularly fats and carbohydrates, as soon as body weight exceeds, say, 10% of what it was when the person stopped growing.

[1] Metchnikoff, E., *The Prolongation of Life*, 1908, New York and London.
[2] Silberberg, M., and Silberberg, R., *Physiol. Rev.*, 1955, **35**, 347.
[3] Riesen, W. H., Herbst, E. J., Walliker, C., and Elvehjem, C. A., *Amer. J. Physiol.*, 1947, **148**, 614.
[4] Slonaker, J. R., ibid., 1931, **98**, 266.
[5] French, C. E., Ingram, R. H., Uram, J. A., Barron, G. P., and Swift, R. W., *J. Nutr.*, 1953, **51**, 329.
[6] Robertson, T. B., and Ray, L. A., *J. biol. Chem.*, 1919, **37**, 427.

ABRASIVE TREATMENT OF ACNE SCARS

Early in this century Kromayer used rotating knives for the removal of skin blemishes and later applied the technique to the removal of tattoo marks and disfiguring scars such as may be caused by smallpox. Others have taken up these methods of treatment, and for a while the use of sandpaper in an abrasive technique was widely explored, but it carried a small risk of leaving silica particles in the skin, which might later give rise to foreign-body granulomatous reactions. In recent years revolving steel-wire brushes driven by a dental motor have largely replaced these earlier measures. Dermatologists in America and the Commonwealth are advocating this abrasive treatment for scars which may follow acne or other skin diseases.

Acne vulgaris is itself a troublesome and depressing affection for the adolescent, though the response to treatment of the majority of patients is good. Some, however, prove very intractable and may be left with pitted scarring quite as disfiguring as the scars from

[1] Eller, J. J., *New Engl. J. Med.*, 1955, **253**, 11.

smallpox and as distressing to the patient as the acne itself. The results of treatment with revolving steel-wire brushes in the hands of the experienced are good, but the procedure has its surgical aspect and is more likely to be practised by the plastic surgeon in this country, as is already happening. The area to be "planed" with the revolving brushes, after preliminary cleansing, is frozen with ethyl chloride. The operator abrades the treated areas using a circular or saucering motion, with a pressure and to a depth learned by experience. After oozing has ceased, the parts are dressed daily until healing occurs in the course of a week to ten days. The procedure is repeated if necessary at monthly intervals for three or four treatments.

There is little or no pain associated with the procedure. The speed of the revolving brush bears upon the ease and effectiveness of treatment, and Belisario, whose method is described above, prefers a machine giving 12,000 revolutions per minute. Reactions are unusual, and the development of hypertrophic scars is apparently very rare. J. J. Eller,[1] who now uses heatless grinding stones and a motor capable of developing 30,000 revolutions per minute, has recently reported impressive results. He sometimes avoids the freezing technique, using local analgesics instead. There is obviously a place for these measures in cosmetic dermatology.

SALMONELLA SUBTLETIES

One of the most striking features of the salmonella group of organisms is the wide range of symptoms which they can produce. At one extreme is the acute food-poisoning characteristically caused by organisms such as *Salmonella typhi-murium* (*aertrycke*), *Salmonella enteritidis* (*gaertner*), and many other members of the genus. At the other extreme is the long-continued illness of enteric fever caused characteristically but not uniquely by *Salmonella typhi* and having the features of a systemic even more than an alimentary infection. But many salmonellae can play a dual role, and *Salmonella paratyphi B* has long been known for its capacity to produce from time to time symptoms of acute food-poisoning as well as of enteric fever.

A series of recent papers gives an interesting account of acute food-poisoning outbreaks caused by unusual members of the salmonella group related to *Salmonella paratyphi B*.[1-3] In the first of these papers R. D. Gray and Sadie Harvey describe an outbreak which occurred at the end of 1951 in a residential nursery maintained by Monmouthshire County Council. Two children (a sister and brother) with an unusually persistent gastro-enteritis were found to be excreting the causal organism, which was also isolated from 15 of 22 children, and 3 of 16 adults, all of whom were free of symptoms. Although the source of infection was not discovered for certain, the same organism was isolated from the faeces of a farmer who supplied raw tuberculin-tested milk to the nursery and who had himself had a short, sharp attack of "gastritis" four days before the first of the two children fell ill in the nursery.

In the second paper J. Grant and R. Norton describe a small outbreak of gastro-enteritis affecting a number of households on South Tyneside. Twelve households were affected, containing 49 persons, of whom 14 had clinical symptoms and 17 were symptomless excreters of the same salmonella. The main clinical features were sudden onset of cramp-like abdominal pain and vomiting, followed by severe diarrhoea lasting from two to eight days. The onset of illness in half the cases occurred during the week-end May 29 to June 2, 1954. The last patient developed symptoms on June 26, 1954; no fresh cases or carriers were found in the following two months. The origin of the outbreak was not determined.

In the third paper J. C. McDonald, Audrey Price, and Joan Taylor review the epidemiological and bacteriological features of these and other similar infections. The organism has been isolated so far from 99 persons—43 with symptoms, 56 without. Cases occurred in three waves—in December, 1951, to February, 1952, in March to July, 1953, and in March to June, 1954. Forty-two of the 43 patients had diarrhoea, which in some of them was severe. The illness usually had a sudden onset and lasted two to four days, but in some patients diarrhoea persisted for several weeks.

The bacteriological results were interesting. The organisms all behaved like typical salmonellae and closely resembled *Salmonella paratyphi B*; but they differed biochemically from it in failing to ferment dulcitol even after three weeks' incubation, in fermenting D-tartrate, and in failing to produce the slime wall characteristic of the growth of *Salm. paratyphi B* in certain conditions. The most striking difference perhaps was in antigenic structure. Whereas the somatic (O) and phase 1H antigens appeared to be the same as in typical *Salm. paratyphi B*, phase 2H antigens could not be detected. The organism thus seems to be monophasic, with the antigenic structure IV, V, XII: b,-. The authors point out that this organism is very like *Salm. paratyphi B.* var. *java*, now named *Salm. java* by F. Kauffmann,[4] but suggest that, in view of certain points of difference, it may perhaps deserve to be recognized as a separate salmonella type. M. Kristensen,[5] however, who as early as 1929 described a special group of organisms with precisely the same characters, is firmly of the opinion that this group of organisms is in fact *Salm. java* and not a new type. This is clearly one of the finer points of salmonella taxonomy which it must be left to the experts to settle. But, however that may be, these recently described outbreaks of food-poisoning show clearly the need for close co-ordination of clinical, epidemiological, and bacteriological investigations in the control of infectious disease. The laboratory can play its proper part in such investigations only if there are opportunities both locally and centrally for the rapid and accurate identification of unusual as well as usual agents of infectious disease. These outbreaks show clearly how admirably an organization such as the Public Health Laboratory Service provides these opportunities.

[1] Gray, R. D., and Harvey, S. M. R., *Monthly Bull. Minist. Hlth (Lond.)*, 1955, **14**, 74.
[2] Grant, J., and Norton, R., ibid., 1955, **14**, 79.
[3] McDonald, J. C., *et al.*, ibid., 1955, **14**, 83.
[4] Kauffmann, F., *Enterobacteriaceae*, 2nd ed., 1954, Copenhagen.
[5] Kristensen, M., *Lancet*, 1955, **2**, 91.

EMERGENCIES IN GENERAL PRACTICE

DANGEROUS BRONCHITIS

BY

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The importance of bronchitis as a cause of morbidity and mortality needs no emphasis: in England and Wales in 1950 590,000 spells of incapacity from work and 28,000 deaths were attributed to this cause. With few exceptions,* acute bronchitis becomes a serious illness only in patients with pre-existing impairment of respiratory function—those with chronic bronchitis, emphysema, pulmonary fibrosis, severe chest wall deformity, or heart disease. In such subjects an exacerbation of bronchitis may precipitate acute respiratory failure with generalized impairment of the ventilation of the lung alveoli. Carbon dioxide accumulates in underventilated alveoli, with a consequent fall in oxygen tension. The blood leaving such alveoli is not fully oxygenated and has a high carbon-dioxide tension which causes a shift of blood *p*H toward the acid side. This triad of carbon-dioxide retention, anoxaemia, and acidaemia—which may be demonstrated by arterial blood analysis—characterizes respiratory failure.

Pathogenesis of Respiratory Failure

How does respiratory failure arise during acute chest infections? A complete answer would require a lengthy digression into the realms of respiratory physiology, but, in brief, there are two principal causes.

(1) *Impaired Sensitivity of the Respiratory Centre.*—Respiratory infection may initiate a vicious circle: pulmonary infection→arterial anoxaemia→anoxic damage to the medullary respiratory centre→diminished drive to the respiratory muscles→alveolar hypoventilation→carbon-dioxide retention→further increase in arterial anoxaemia. This sequence of events is particularly apt to occur in the chronic bronchitic or emphysematous subject who—even when free from respiratory infection—is chronically anoxic and shows a diminished respiratory response to inhalation of carbon dioxide. Treatment is based on oxygen therapy, which prevents further damage to the respiratory centre, together with the use of respiratory stimulants.

(2) *Increased Metabolism and Reduced Ventilatory Capacity.*—Increase in metabolic rate may be due, in part, to fever, but more specifically to the greater energy expended by the respiratory muscles working under difficulties. Bronchiolar obstruction (by oedema, spasm, or mucus) and pulmonary consolidation greatly increase the amount of work that must be done to get a given volume of air in and out of the lungs. This increase in ventilatory work causes an increase in metabolism, and thus the lungs have a larger volume of carbon dioxide to excrete—and this requires a greater ventilatory effort. Thus, a point may be reached where the increase of carbon-dioxide production by the increased work of the respiratory muscles begins to outstrip the consequent increase of alveolar ventilation. Further attempts to increase ventilation will then actually increase the alveolar carbon-dioxide tension. Severe status asthmaticus exemplifies this type of respiratory failure. Effective methods of treatment are those that lower the metabolic rate and relieve the obstruction to ventilation: bed rest and chemotherapy will control bronchial infection and lower the temperature; bronchodilators will relieve respiratory obstruction and diminish the work of breathing. In practice, respiratory failure is usually due to a combination of both mechanisms.

*Pertussis and other types of bronchitis in babies and young children will not be considered in this article.

Clinical Picture of Bronchitis with Respiratory Failure

The clinical picture of uncomplicated bronchitis is familiar to all: following exposure to "smog," or after a head cold, influenza, or other infections of the respiratory tract, the patient develops an irritating cough, substernal soreness made worse by deep breathing, wheeziness, and moderate pyrexia. The cough, at first dry, soon becomes productive of purulent sputum. There is little or no dyspnoea; the mucosae show no trace of cyanosis, and mental disturbance (apart from the delirium of pyrexia) does not occur. With the development of respiratory failure, however, new symptoms and signs appear: these can all be attributed to the effects of carbon-dioxide retention, anoxaemia, and acidaemia on the brain, cerebral vessels, lung, heart, and kidneys.

Cyanosis is the outward and visible sign of arterial oxygen unsaturation. It is usually impossible to detect cyanosis of central origin clinically until the arterial oxygen saturation has fallen to 80–85%, and anaemia may mask its appearance entirely. Increasing cyanosis during an attack of bronchitis signifies the development of respiratory failure or that bronchial infection has spread to the alveoli, causing patchy consolidation (or, more usually, both these events). Mental disturbance varies from mild disorientation to restless delirium, stupor, and even unrousable coma. An attack of bronchitis may manifest itself as undue drowsiness—the patient falling asleep at work or over his evening meal.

If a chronic bronchitic suddenly develops an acute psychosis with visual and auditory hallucinations or paranoid delusions, an acute respiratory infection is the most likely cause and such patients should be sent to a general hospital rather than an observation ward. Characteristically, the mental state fluctuates from hour to hour, and a patient who was disorientated during the morning may become sufficiently alert to converse rationally when his doctor calls later in the day.

Cerebral vasodilatation causes a rise of intracranial pressure, and the associated throbbing headache may be severe enough to prevent sleep. The retinal veins are always dilated, and frank papilloedema with swelling of the nerve head and flame-shaped retinal haemorrhages may occasionally be seen. Muscular twitching is a characteristic feature of respiratory failure. This consists of coarse, irregular, jerky movements of the fingers, arms, and, less frequently, of the muscles of the face, trunk, or legs. In patients with pre-existing right ventricular hypertrophy and stress, respiratory failure is the commonest cause of congestive cardiac failure. We do not exactly know how this comes about, but it has been shown that anoxia and hypercapnia raise the pulmonary artery pressure by constriction of the pulmonary arterioles; that anoxia and acidaemia increase cardiac output; and that fluid retention and increase in blood volume are a sequel to diminished renal blood flow and increased tubular reabsorption of sodium. Peripheral vasodilatation is recognized clinically by warm hands, large volume pulse, capillary pulsation in the nail beds, and an increased pulse pressure.

Differential Diagnosis

Experience has shown—in both hospital and general practice—that bronchitis with respiratory failure is often misdiagnosed as left ventricular failure with pulmonary oedema. This mistake can have serious consequences, since the administration of morphine—the drug of choice in treating

pulmonary oedema—often proves rapidly fatal when given to a patient in respiratory failure. The main differential points are tabulated below :

Bronchitis with Respiratory Failure	*Left Ventricular Failure*
Previous history of chronic cough, sputum, increasing dyspnoea on exertion, and recurrent bronchitis for 10 or more years.	Chronic cough not usually prominent in the history. Known to be hypertensive or to have other heart disease.
Rapid, shallow, gasping respirations—often irregular in rate and depth—but never periodic. Many deeply cyanosed patients are able to lie flat without discomfort.	Dyspnoea always severe ; unable to lie flat. Respirations often periodic in character (Cheyne-Stokes).
Usually pyrexial (especially if temperature is taken rectally).	Rarely pyrexial.
Purulent sputum ; may be difficult to expectorate.	Frothy, watery, blood-tinged sputum.
Retinal veins dilated ; occasionally papilloedema.	Normal fundus, or changes of hypertensive retinopathy.
Epigastric heave indicating right ventricular hypertrophy.	Apical heave indicating left ventricular hypertrophy.
Warm extremities ; large volume pulse.	Peripheral vasoconstriction with cold hands.
Arm-tongue circulation time normal or even accelerated.	Arm-tongue time much prolonged.
Arterial plasma carbon-dioxide content raised (more than 66 vols.%).	Arterial plasma carbon-dioxide content normal or reduced.

When acute bronchitis precipitates left ventricular failure —as it often does in the elderly hypertensive—it may be exceedingly difficult to decide which is the more important condition. If there is any doubt, it is wiser to withhold opiates and pursue lines of therapy suitable to both conditions.

Antibiotic Therapy

Antibiotic therapy is the most important single measure in treatment. Before starting treatment a specimen of purulent sputum should be sent for bacteriological examination and the sensitivity to antibiotics of any pathogens isolated determined. Treatment should, of course, be started at once without waiting for the laboratory report. Numerically, *Streptococcus pneumoniae* and *Haemophilus influenzae* are the two most common pathogens, and will be found in from 70–90% of cases ; less common pathogens include *Staphylococcus pyogenes*, *β*-haemolytic streptococci, *Pseudomonas pyocyanea*, Friedländer's bacillus, *Proteus vulgaris*, and *Bacterium coli*. *H. influenzae* is not (or is only partially) sensitive to penicillin, but is usually sensitive to streptomycin, the tetracyclines, and chloramphenicol.

In uncomplicated bronchitis it is justifiable to give 900,000 units of procaine penicillin daily, and, if necessary, to alter treatment after three to five days if the clinical response is unsatisfactory and sputum culture reveals a penicillin-insensitive pathogen. However, in severe bronchitis with respiratory failure, time is precious, and even 24 hours' delay in controlling the bronchial infection may tip the scales against recovery. Therefore, treatment effective against all the common bronchial pathogens should be started immediately. In hospital practice the treatment of choice is a combination of crystalline penicillin and streptomycin intramuscularly: penicillin 500,000 units and streptomycin 1 g. six-hourly for two days, followed by the same dosage 12-hourly for a further five to eight days or until the sputum has become mucoid. In general practice it may not be possible to arrange for frequent intramuscular injections, but a wide range of oral antibiotics is now available : chlortetracycline, oxytetracycline, and tetracycline—a loading dose of 1 g. followed by 0.5 g. six-hourly for two days, then 0.25 g. six-hourly for a further five to seven days—are all more or less equally effective. The drug of choice is tetracycline itself, since there is evidence that it gives rise to fewer side-effects than the other antibiotics. Chloramphenicol, although highly effective, should not be used in treating acute exacerbations of bronchitis in chronic bronchitic subjects, since further courses of treatment will almost certainly be required at a later date and aplastic anaemia becomes an increasing hazard when a total dose of more than 20–25 g. has been administered.

All the wide-spectrum antibiotics have one serious disadvantage : a fulminating enterocolitis may occur even after small doses and prove rapidly fatal in an ill patient. For this reason I advise a combined course of penicillin and streptomycin whenever facilities for frequent intramuscular injection can be arranged. The toxic effects of streptomycin are less serious : labyrinthine damage may occur in the elderly or in those with renal failure, but is unlikely after only a short period of administration. Clinically, any significant degree of renal impairment can be virtually excluded by the absence of albuminuria and a urinary specific gravity of more than 1020 in a casual specimen. Streptomycin should *never* be given to elderly patients in a dosage of 4 g. a day for more than three to four days and the total amount should not exceed 20 g. *In vitro*, most strains of *H. influenzae* are sensitive to sulphonamides, but the clinical response of *Haemophilus* bronchitis to these drugs is, unfortunately, often disappointing.

Bronchodilators

If respiratory failure is principally due to air-way obstruction intensive and sustained antispasmodic therapy is indicated. Aminophylline should be given by slow intravenous injection of 0.25–0.5 g. at intervals of four to six hours; or as rectal suppositories containing 0.36 g. It is too painful to be administered intramuscularly and usually ineffective when given orally. Solutions of 1:100 isoprenaline, 1:100 adrenaline, or 1:200 phenylephrine are given as an aerosol spray: in hospital from a nebulizer operated by compressed air or oxygen ; and in the home, from a hand inhaler. Inhalations lasting five to ten minutes (with a total dose not exceeding 10 mg.—for example, 1 ml. of a 1:100 solution) should be prescribed at intervals of two to three hours in the acute stage, decreasing to three to four times a day as the patient improves. If signs of overdosage occur—trembling, nausea, vomiting, or palpitations—the dose should be reduced or given more slowly. Isoprenaline is also effective when given sublingually as a 10-mg. tablet at similar intervals. Adrenaline may also be given intramuscularly or subcutaneously as a 1:1000 solution: 0.5 ml. (8 minims) followed by 0.06 ml. (1 minim) every minute until bronchospasm is substantially alleviated. If these measures fail to relieve severe bronchospasm after 24–36 hours, a trial of adrenocortical hormones is warranted : cortisone 50 mg. eight-hourly by mouth, or, alternatively, 20 units of the long-acting corticotrophin gel intramuscularly twice daily. In asthmatic bronchitis benefit is usually apparent within 12–18 hours, and if there is no improvement within 36 hours the drug should be discontinued. If the hormones relieve bronchospasm, treatment should be continued for five to six days, with gradual tailing-off of the dosage.

Bronchial obstruction is often due to viscid, tenacious sputum which the patient finds great difficulty in coughing up. An effective method of liquefying sputum would be of great value, but unfortunately a specific mucolytic enzyme preparation is not available. The effect of synthetic detergents and proteolytic enzymes by aerosol is currently under investigation, and no firm opinion on their clinical value can yet be given. Some patients find that a steam tent or inhalation of friars' balsam gives considerable symptomatic relief. After the inhalation of a bronchodilator, postural drainage with percussion of the chest wall will help clear the bronchial tree of secretions. There is a widespread belief that mixtures containing potassium iodide or ammonium carbonate liquefy sputum and aid its expectoration. Careful studies of these so-called " expectorants " have failed to confirm this belief, and their administration should be confined to those patients who feel that they would benefit from a bottle of " cough mixture."

Oxygen Therapy

Oxygen equipment can be prescribed on Form E.C.10. For the administration of oxygen in the home, the inexpensive light-weight plastic " polymask " (made by British

Oxygen Company) can be highly recommended. Most patients tolerate this extremely well, and a tent will be required only for the occasional patient who persists in removing his mask.

Oxygen should never be administered continuously in high concentrations to patients with respiratory failure. If anoxia is completely relieved the main stimulus to respiration is abolished, ventilation falls, and the alveolar carbon-dioxide tension rises still higher. Finally the rising carbon-dioxide tension and acidaemia cause coma, falling blood pressure, and irreversible medullary depression. Carbon-dioxide narcosis can often be avoided by administering oxygen by either of two techniques: (*a*) continuously at low rates of flow (1–2 litres per minute)—the flow rate should be adjusted so that the nail beds and mucosae still show the faintest tinge of cyanosis; or (*b*) in high concentrations intermittently. This may be done by giving oxygen at 6–8 litres per minute by tent or mask for 20 minutes, and then allowing the patient to breathe room air for 15 minutes. By this means, carbon dioxide retained during the period of breathing oxygen will be washed out again as ventilation increases on breathing air, and a progressive rise in the arterial carbon-dioxide tension is prevented. The careful use of oxygen therapy will prevent many bronchitic patients dying from the effects of severe anoxaemia.

Management of Heart Failure

Minor degrees of congestive cardiac failure need no specific treatment, since, if the bronchial infection can be brought under control and respiratory failure reversed, raised venous pressure and oedema will disappear spontaneously.

If the venous pressure is very high or oedema persists despite adequate treatment of the bronchitis, digitalis in full dosage, mercurial diuretics, and a diet low in sodium should be prescribed. Mersalyl, 2 ml., should be given intramuscularly on alternate days; albuminuria is not a contraindication to its use, since this usually disappears with improvement of the heart failure. Repeated venesection of one to two pints (0.6 to 1.1 litres) may be helpful in the rare cases in which chronic congestive failure is associated with polycythaemia.

Analeptics and Sedatives

From time to time the practitioner will be called to a patient *in extremis*: deeply cyanosed, comatose, with shallow, ineffective, gasping respiration. This emergency demands immediate treatment: 10 ml. of nikethamide and 0.5 g. of aminophylline should be given intravenously, and oxygen by mask at 6–7 litres per minute. The effect will be dramatic: within ten seconds the patient sits up, recovers consciousness, and coughs vigorously. The effect wears off in 20–30 minutes, but nikethamide is metabolized extremely rapidly and a similar dose can be repeated at intervals of one to two hours until the patient is out of danger. Nikethamide is ineffective when given by mouth.

On no account should opiates or barbiturates be administered to these patients. This point cannot be emphasized too strongly. Even 100 mg. (1½ gr.) of butobarbitone may cause severe respiratory depression with prolonged coma, while 10 mg. (1/6 gr.) of morphine may be fatal. The depressant effect of morphine, methadone, and pethidine can be immediately reversed by the intravenous injection of 10–20 mg. of nalorphine. No emergency bag should be without this useful drug. If sedation of an extremely restless patient is required, the drug of choice is paraldehyde, which has only a slightly depressant effect on the respiratory centre. The dose is 5 ml. intramuscularly; it should not be repeated.

Respiratory failure is a serious complication of bronchitis and is best treated in hospital. However, during periods of fog or epidemics of influenza a hospital bed may be unobtainable and the practitioner will be required to treat these patients at home to the best of his ability. An understanding of the basic disturbances of respiratory physiology will make this task easier.

Next article on Emergencies in General Practice.—"Coma in Hypopituitarism," by Professor H. L. Sheehan.

Refresher Course Book.—Copies of the second volume of collected articles from the Refresher Course for General Practitioners are still available at 25s. (postage 1s.) each. The first volume is now sold out.

Clinical Pathology Book.—"Clinical Pathology in General Practice," a collection of 39 articles on clinical pathology that appeared in the *Journal* as part of the Refresher Course for General Practitioners, is now available, price 21s. (postage 9d.).

Both these volumes are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or through any bookseller.

OSLER MEMORIAL AT OXFORD

The Osler Club has placed a memorial plaque on the outer wall of the house at Oxford (13, Norham Gardens) which was occupied by Sir William Osler during his 12 years as regius professor of medicine and in which he died in 1919. It was unveiled on October 8 by the regius professor-designate, Professor G. W. PICKERING, before an assembly which included many distinguished physicians and surgeons.

Mr. V. B. GREEN-ARMYTAGE, president of the Club, said that he was one of the diminishing band who knew Osler; 50 years ago, almost to the day, he received a prize at his hands. The Osler Club in London was founded in the 'twenties by six of his students. Before the second world war the Club had a difficult time, although people of the eminence of Lord Horder, Sir Farquhar Buzzard, Sir Walter Langdon-Brown, and others came to address it, but after the war, in 1947, it was revived, thanks to the efforts of three men, Dr. L. Carlyle Lyon, Dr. A. White Franklin, and its present secretary, Dr. W. R. Bett. It now had 152 members.

Time for the Young

Professor PICKERING said that it was just 50 years ago that Osler came to Oxford from Baltimore. The house in which he lived was intended to be the residence of regius professors of medicine, but for one reason or another none of his successors had lived there. Perhaps some of them felt that a house of 14 bedrooms was beyond the needs of an ageing professor. But thanks to the efforts of Professor A. D. Gardner, who was still acting regius professor, Osler's original purpose was to be in part fulfilled. The house was to be converted into flats, in one of which the future regius professor would live.

Why was Osler commemorated in Oxford? Undoubtedly his great work was accomplished on the North American continent. He served successively McGill, the University of Pennsylvania, and Johns Hopkins. If he was not the creator of Johns Hopkins Medical School, he was the chief instrument in its creation. The Johns Hopkins Hospital laid down a pattern for a teaching hospital and medical school that was destined to be followed by every teaching institution in the United States. Probably no other institution in the world had had such a direct effect on medical education. It was in North America, too, that Osler did his great scientific work, carrying out original and valuable researches on diseases of the spleen and blood and infections of the heart, and it was there he wrote his textbooks in which the facts of clinical medicine were set out in so orderly a manner.

Osler was 56 when he came to Oxford, and, judging from his letters, he had no intention of working at the same pace. But the Medical School gained distinction under his leadership, and he was also curator of the Bodleian Library, delegate of the University Press, and participant in many aspects

of university life as well as in the general medical and public life of the country. But many others had done as much. Why was there an Osler Club, and why was the student house of the University named Osler House? No other figure in the world of medicine during the last 50 years had had his memory perpetuated in the same way. Perhaps it was his versatility—a great physician, a great teacher, a great scholar—but Professor Pickering believed that the answer lay in Osler's appeal to the young. Universities were and always would be the province of young men and women. Throughout his immensely busy life Osler remained at heart a boy, with his enthusiasm and impish humour. He never acquired that pomposity which so often separated the ageing and old from the young. He always had time for the young man's problem, which he understood more clearly than the young man himself. It was because he always had time for his students and was remarkably like them himself that the Osler tradition persisted.

Professor Pickering then unveiled the plaque, which simply recorded the dates of Osler's residence in the house, and a vote of thanks was accorded to Professor Pickering on the motion of Dr. W. R. BETT.

RENAL DISEASE

SYMPOSIUM AT POSTGRADUATE MEDICAL SCHOOL

A symposium for consultants on "Modern Aspects of Renal Disease" was held in the Postgraduate Medical School of London from September 26 to 30. Professor J. R. SQUIRE (Birmingham) showed that in acute nephritis the electrophoretic pattern of urinary proteins was the same as that of the plasma proteins, but in nephrosis the urine contained a far higher proportion of albumin than of other serum proteins. In nephrosis cortisone might reduce the leakage of albumin. Dr. REGINALD LIGHTWOOD emphasized that cortisone and A.C.T.H. in nephrosis were largely symptomatic measures. The prospects of complete (three-year) cure were only slightly improved, since this could occur in about one-sixth of the cases without hormone treatment. Dr. M. D. MILNE described the varied pathogenesis of the nephrotic syndrome and showed examples due to renal-vein thrombosis. A patient with rheumatoid arthritis and renal amyloidosis was showing signs of improvement of the kidney condition on cortisone. Professor CLIFFORD WILSON spoke of the occasional possibility of recovery from type 1 and type 2 nephritis after an illness of a year or two, especially if there was no hypertension.

Pyelonephritis

Professor M. ROSENHEIM said that chronic pyelonephritis was often very difficult to recognize in the absence of causative factors or a clear history of acute attacks. Albuminuria was likely to be intermittent, and bizarre disorders of tubular function—for example, salt losses—often resulted. Careful study of pyelograms was necessary. Treatment with sulphonamides should be continued until the urine remained sterile, when the drug was discontinued. Dr. P. KINCAID-SMITH said that 17% of 130 kidneys from malignant hypertensives were pyelonephritic. All but one of the patients under the age of 30 had nephritis or pyelonephritis. Mr. R. SHACKMAN, basing his remarks on a small but carefully studied series of divided renal clearance studies, thought that hypertension was more likely to be relieved by removing a pyelonephritic kidney with some residual function than by removing a functionless scarred kidney.

Discussing chronic uraemia, both Dr. D. A. K. BLACK and Professor ROSENHEIM regarded as of prime importance the correction of extrarenal factors (circulatory, infective, gastro-intestinal, etc.), which might impair renal function. Dr. S. W. STANBURY emphasized in particular the damaging effects on the kidney of administration of calciferol in "renal rickets." Dr. LIGHTWOOD mentioned that vitamin D was often added to proprietary cereals, and this unknown medication was potentially harmful.

Acute Anuria

The treatment of acute anuria was discussed by Dr. K. G. LOWE. In many mild cases oral lactose and water, to supply 800 to 1,000 calories per day, was probably all that was necessary. The administration of ion-exchange resins in the sodium cycle as retention enemata could be used to lower the blood potassium. Dr. J. HAMBURGER (Paris) demonstrated the results obtained at the Hôpital Necker with a new modification of Kolff's artificial kidney. After six hours on the machine blood urea fell in one case from 540 to 90 mg./100 ml. with full correction of disturbed electrolytes. He was convinced that some patients too hopeless for conservative measures could recover with this new method.

Dr. C. E. DENT discussed some syndromes of renal tubular insufficiency, particularly Fanconi's syndrome of phosphaturia and amino-aciduria. In this and allied disorders failure of the kidney to reabsorb phosphorus might lead to secondary disturbances of calcium metabolism and "resistant" rickets or osteomalacia. These conditions were also discussed by Professor R. A. MCCANCE and Dr. LIGHTWOOD.

Electrolytes

The role of electrolytes in renal disorders was discussed by Dr. D. A. K. BLACK. In renal disease the acid-base balance could be disturbed, and sodium and potassium could be lost by defective tubular function. Sodium depletion in turn could impair the renal circulation; alkalosis with a high calcium intake (the "milk–alkali syndrome") could damage the kidneys directly. Where there was both sodium and potassium depletion it was a good practical measure to correct sodium deficiency first, so that kidney function was as good as possible before giving potassium. Professor MCCANCE spoke of "steady states" reached in various oedematous conditions, and emphasized the difficulty of knowing what changes were taking place inside the living cells of the body. Dr. M. D. MILNE deplored the giving of saline to oedematous patients even though sodium concentration might be low, for under these conditions the body already contained much more than the normal amount of sodium.

Dr. PAUL FOURMAN spoke on potassium depletion from gastro-intestinal and renal loss, etc. Clinical effects might be slight—constipation, apathy, and weakness. Response to treatment was usually early and striking, but potassium salts given intravenously should be given slowly—not more than 80 mEq/litre/4 hours.

Diuretics

Dr. R. I. S. BAYLISS emphasized that the efficacy of mercurial diuretics depended on an adequate load of chloride, which could be given entirely as ammonium or partly as potassium salts. Low sodium concentrations in cardiac patients did not necessarily result from excessive use of diuretics but were rather an expression of illness. Dr. MILNE discussed acetazoleamide ("diamox"), which promoted the excretion of bicarbonate, at first combined with sodium but later with potassium. This was not a suitable diuretic for routine use, but it might be used as an adjuvant to mercurials provided potassium loss was made up.

Dr. OLIVER GARROD reviewed the aetiology of diabetes insipidus, and Dr. C. L. COPE gave a brief account of the action of hydrocortisone and aldosterone, both of which cause excessive potassium loss.

Among a variety of interesting demonstrations Dr. R. MUEHRCKE (Chicago) showed lesions which could be demonstrated and followed serially by needle biopsy of the kidney, a procedure which was free of trouble in the 357 cases to which it had been applied. Dr. I. GILLILAND demonstrated the technique of retroperitoneal air insufflation as an aid in giving better radiological delineation of the kidneys. Dr. E. M. DARMADY showed the results of detailed microdissection of the renal tubules. Dr. E. G. L. BYWATERS demonstrated the kidney lesions in "collagen disorders," and Dr. R. SOUGIN-MIBASHAN (Capetown) gave a full analysis of the kidney disorders in gout.

NEW ACADEMIC YEAR

UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL

The opening ceremony of the session at University College Hospital Medical School took place on October 4, when an address was given by Sir GEOFFREY JEFFERSON, F.R.S., and prizes were presented by Lady Jefferson. The chair was taken by Sir CHARLES HARINGTON, F.R.S., chairman of the School council.

Sir Geoffrey Jefferson said that during the past five or six years we had come nearer than at any time in our history to obtaining a glimpse of the integration of the brain and the way in which it worked as a whole. Everyone took the acquisition of his own personal store of knowledge so much for granted that thought was rarely given to the ways in which it had been acquired. It was perhaps trite to say that all our knowledge had been won, it had been a personal acquisition, the result of our passage through life. We inherited nothing but instincts; we had no congenital ideas, no inner knowledge, nothing but the machinery to acquire such things. Aristotle was supposed to have remarked that there was nothing in the mind but what had previously made its way there through the senses. To the average man the proposition that that precious possession, his individual mind, was no more than a receptacle came as something of a shock. There were few who would not feel insulted by Aristotle. Was that mind of theirs composed of nothing but the odds and ends of the past—much of it in any case best forgotten? Surely the thoughts that we had were essentially our own inventions, not the pickings from a dust heap.

The speaker said that he sympathized with such protestations, but why was it that whatever inventions we hit upon, whatever the productions of our minds or hands, they were always of the kind to which we had been trained or had trained ourselves? If our minds were capable of pure inventions why did we not add to the sum of human knowledge by some flash of intuitive reasoning far outside our orbit? Discovery was only to be made by those who had put into their heads the material necessary for discovery.

At the same time, Sir Geoffrey continued, no one to-day would hold that all men were born equal in anything but impotence. Could inherent inequalities be erased by education? When he was an undergraduate he thought they could. He had believed that those who found difficulty in learning anatomy or grasping physiological ideas did so because they lacked diligence. How sadly was he mistaken. Yet it was an undoubted fact that teaching did help the willing learner.

The conclusion which seemed to emerge very clearly from this discussion was that we should take care quantitatively and qualitatively what we fed into our minds. In school and university the nature of the input was standardized, but the individual could vary it, and certainly should do so by extra-curricular reading and inquiry. The great ones in human history could not have had anything but conventional educations—he was thinking of men like Newton and Rutherford—yet the conclusions they drew from what they had read or been taught were strictly unorthodox. And there, of course, we had it—unconventionality in thinking was the mark of genius. As long as a man thought along the straight lines his teachers drew for him nothing really new could possibly emerge. Some would lack the insight, the curiosity, the passion to explore an idea; others would be lacking in energy, in the power to pursue thinking with sufficient continuity. It was here that so many failed, because they were lazy or too easily distracted.

The orator admitted that he had not answered the question with which he started—the why or how of the natural inequalities amongst men. Any answer must be purely conjectural. Did brains differ from one another in the number of their cells? Almost certainly they did. We did not know yet for certain because of the immense labour of counting the thousands of millions. But new methods, such as electronic ones of scanning and counting, would give the answer before many years had passed.

"Mechanical though it all very likely is," said Sir Geoffrey in conclusion, "we must not lose sight of the fact that some human beings so manage themselves as to make the words unselfishness, friendliness, even nobility, applicable to their total behaviour. Such things as ethics and morals are important in human affairs. So we must each of us learn to make the best of the abilities which our genetic inheritance has given us and try to steer this potentially treacherous machine through life as best we may."

The Dean, Dr. J. D. S. FLEW, in his report, said that the School had an embarrassingly large number of undergraduates. Many of the students had financial assistance from State and county scholarships, but there were some whose parents, at least in theory, were so well off that it was considered that they needed no financial assistance in the education of their children. Nothing, of course, was further from the truth, and in many cases great hardship was endured by such parents. He reported the donation of a scholarship by Mr. G. F. C. Croxon to enable a student who was obtaining little or no financial assistance from other sources to complete his or her medical education. This would bring in some £380 a year. Dr. Flew added that his own first year as Dean was now complete and the School had proceeded serenely on its way without undue catastrophe. This was entirely due to those who had helped him, and he publicly expressed his appreciation in particular of the Vice-dean, Professor S. J. Cowell, and the Secretary, General Birks, and all who had worked in the administration. With very great regret he had to inform them of the retirement next year of Professor Cowell, who as Vice-dean during the past years had done so much for the School: they were all deeply indebted to him.

WESTMINSTER MEDICAL SCHOOL

Welfare State

The inaugural address of the session of the Westminster Medical School was delivered on October 3 by Air Marshal LORD TEDDER, Chancellor of Cambridge University, who also distributed the prizes.

Lord Tedder recalled a remark of Samuel Butler: "A skilful leech is better far than half a hundred men of war"—a discouraging thought for himself in facing a medical audience, knowing that in their speech he was referred to as a layman, with the implication of being someone outside a learned profession. However, the word "layman" was derived from a Greek word meaning "the people," and "that is just what we are; and, after all, where would you be without us, and, for that matter, where should we be without you?" He would like to see a historical study made of the relationship through the ages of the doctor and the layman, between the medicine man and the victims of his magic, between the family doctor and his patient, and between the National Health Service practitioner of to-day and those on his list.

The whole shape of society in the Western hemisphere had changed in recent decades, and not every nation had stood up to the stresses and strains of modern times. He believed that the British people had a rugged individuality, coupled with a keen sense of personal responsibility. At the same time one must not be over-complacent. He might have been unfortunate, but lately he had encountered many instances of refusal to take responsible positions—the National Service man refusing to take a commission, the good craftsman refusing election as shop steward—and the same thing applied to senior people. Was it possible that the kind of democracy nurtured by the Welfare State was to blame for evasion of leadership? Was it bringing about a society of automation like that in factories? He mentioned the case of an expectant mother who decided to have her child under the aegis of the National Health Service. She went to the clinic and had a regular and thorough series of pre-natal

examinations by different specialists. Everything was most successful and the child "came off the production line" in excellent shape, but the mother had been uninstructed in maternal care. Was there not something to be said for the old-fashioned general practitioner dropping in occasionally to check up and giving sound advice based on his long experience? In a national service the lay patient was liable to lose his identity and to become another "case" with an incomprehensible Latin name. If the medical services became dehumanized, then individuality and personal responsibility would fade out, and the laity would become little better than a herd of cattle.

The Dean of the School, Mr. H. M. HARDING, in his annual report, said that there were far more applications for admission to Westminster than could be entertained. Nine out of every ten must be rejected; of those rejected fewer than one-third might find vacancies elsewhere. He complained, as he had done the previous year, about the standard of literary English in papers submitted in the entrance examination. There were good scholarship standards in basic sciences, but a deficiency in English. He thought that the educational institutions should devote more attention to language as literature for those making medicine their career. Some fears had been expressed lately about whether the saturation of the profession had been reached. From his own survey of Westminster men he found no evidence of unemployment or of failure of former students to obtain suitable posts either in general practice or in the specialties. As to the extension of the School, he was hopeful that by the end of the coming quinquennium they would have complete plans for building a new school.

CHARING CROSS HOSPITAL MEDICAL SCHOOL

Arduous Course of Training

The inaugural ceremony of the new session of Charing Cross Hospital Medical School was held at the Royal College of Physicians on October 7, with LORD INMAN presiding, when Major LLOYD GEORGE, M.P., gave a brief address, and Mrs. LLOYD GEORGE distributed the prizes.

The Dean, Dr. E. C. WARNER, gave an account of the events of the school year, the distinctions gained, and the changes in staff personnel. The intake of students was 45 per annum, but no vacancies were filled until students of the required quality presented themselves. During the three clinical years of study the School tried to give the students a good theoretical and practical grounding in general medicine. During the last months of their course they were sent to spend some time working with a general practitioner, and the School was very grateful to the general practitioners who had co-operated. The students also had periods of residence at the associated hospitals. Dr. Warner added that during the year the results of the final examinations in medicine, surgery, and midwifery had reached an unusually high percentage of passes, and he doubted whether any other school in the University could produce a better showing.

Major LLOYD GEORGE said he appreciated the feeling with which young people entered this great profession, to gain entry to which they had to undergo a course of training which, he supposed, was longer and more arduous than for any other calling. But they had this tremendous satisfaction, that they would be able to follow a profession which devoted itself to the service of mankind. He had no doubt that many of those who had received prizes that afternoon would go to the very top of their profession. But it was obvious that not all could be at the top of this or any other profession, and that should not be a matter of discouragement. After all, the world was made up of ordinary people. Whilst, of course, in medicine, as in other professions and the services, an immense debt was due to the outstanding men who were the leaders of progress, yet without the ordinary man doing the ordinary task those achievements and triumphs would not reach their fulfilment. Surely what really mattered, as he saw it, was not whether some were outstanding but whether the ordinary man did his best with the facilities and equipment which he was given.

A vote of thanks to Major Lloyd George was proposed and seconded respectively by Dr. F. A. ELLIOTT and Dr. J. HAMILTON, a visiting Canadian student.

BIRMINGHAM MEDICAL SCHOOL

The ceremonies in connexion with the inauguration of the session at Birmingham Medical School took place on October 3, when Professor THOMAS BODKIN, who formerly held the chair of fine arts and was public orator at the University of Birmingham, gave the address.

Professor Bodkin said that twice in his life he had been publicly hailed as a doctor of medicine. One was in Dublin during the rising of 1916, when he was heavily decorated with a Red Cross brassard as a volunteer street guide and stretcher-bearer, and a bevy of fishwives propelled him into a near-by house where he was called upon to assist a young woman who was just about to give birth to a baby and had been hit in the foot by a stray bullet. Fortunately the Rotunda Hospital was only a stone's throw away, and he succeeded in persuading his captors to procure better help than he could render himself. The other occasion was in a London club, where the conversation turned on the Blalock operation, and after he had uttered a couple of relevant comments a famous surgical peer laid his hand on his shoulder and asked, "Where do you practise?"

It was not always as difficult as it was to-day, continued Professor Bodkin, to recognize the doctor among his fellow creatures. When he was a youth in Dublin most of the doctors wore frock coats and tall silk hats, their waistcoats were invariably adorned with heavy watch-chains, and they signalized their presence with a slight but not unpleasant whiff of perfume. They rode a brougham in winter and a victoria in summer. Not until he was grown up did he realize that hidden away in the back streets of the capital and in the towns and villages were thousands of other doctors labouring with great devotion and small reward. They had little or no private practice, most of them were "dispensary doctors," and they supplemented their official salary of about £300 a year in many cases by running a small farm.

The vocation of medicine was rooted in fortitude and pity. In one respect only were doctors pitiless—they showed no mercy to the offender who attempted to do their work without possessing qualifications. They were inclined to think that no layman could ever show any natural ability in their art and science. Yet how often they read of a policeman or bus conductor who skilfully, in the most septic surroundings, delivered the unexpected baby. Did the doctors honour him and give him a diploma or even excuse him a term of his course should he afterwards elect to seek qualification?

"My fellow patients and myself," Professor Bodkin concluded, "are often more than a little fearful of what the doctors may do to us when we find ourselves completely in their power. We hope they will never forget that they are there to serve rather than to rule us. We beg them, with confidence and gratitude, to bring what healing they can to our bodies and health to our minds, while taking all possible precautions against the risk of harming, unwittingly, our souls. Doctors should always remember that every single one of their patients will die some day, and that the most important hour of life is the last. Warn us of its approach. Help us to face it with fortitude. Preserve our faculties to the utmost. Do not let pity ever tempt you to forget what immense spiritual profit we may draw from suffering. Encourage us in our efforts to earn it."

The Dean, Professor A. P. THOMSON, reviewed the activities of the School and the changes of staff. He paid a tribute to the late Stanley Barnes, whose interest in the School was preserved to the very end of his life, and who bequeathed to it the residue of his estate to complete the building. His generosity, with that of other benefactors, would enable them to build the library and large lecture theatre as they were originally designed and set free space for adequate common-rooms. The building of the second

part of the department of clinical research had been made possible by the help of the teaching hospital and the British Empire Cancer Campaign. The relations of the School with the teaching hospital and the regional board continued to be cordial, and he gladly acknowledged the help which the School had received from both authorities, mentioning in particular the addition to the clinical research block, the metabolic unit at Little Bromwich, and the Day Hospital at Uffculme.

MEDICAL PROTECTION SOCIETY

63rd ANNUAL GENERAL MEETING

The annual general meeting of the Medical Protection Society was held at Victory House, Leicester Square, London, on October 6, Sir Ernest Rock Carling presiding.

In presenting the annual report of the council Sir Ernest Rock Carling said that the Society continued to make good progress. The membership had increased, and so had the number of cases dealt with, but he thought it could be said that they had been conducted to a satisfactory stage. There had been some changes in the law. The alteration of the time within which actions might be brought against a public authority would leave them rather longer in doubt about what their commitments might be, and the change from six years to three years in respect of actions against individual practitioners might affect them a little in the other direction. The alteration in amounts to be claimed in county courts, and the extension to county courts of legal aid, would increase their liabilities.

He must as usual say a word about pitfalls. One was the skin-tight plaster. Cases must be watched with scrupulous care, and the slightest indication of continuing pain or change of colour in the extremities must call for instant attention; if there was any doubt whatever, the plaster must be split or completely removed. Then there was the ever-present question of swabs. He thought it could be said that when a surgeon had made an efficient search for a swab, *secundum artem*, he was entitled to rely upon the organization of the hospital and to appeal to the sister whether the count was correct. He must, however, take proper precautions in the first instance.

Mr. W. M. Mollison, the Treasurer, reported an excess of income over expenditure of more than £7,000 and an increase in the market value of the Society's securities.

The report and accounts were adopted, Sir Ernest Rock Carling was re-elected president, and all the other officers and retiring members of council were also re-elected.

Mr. W. G. Hawkins, of Messrs. Le Brasseur and Oakley, the Society's solicitors, in a brief address, said that the increase in litigation against professional men was generally attributed first to legal aid and secondly to the different relationship between doctors and patients created by the National Health Service. To his mind there was another factor which had led to this increase—namely, the pressure and strain of modern conditions under which professional men had to live and work. One could imagine a busy general practitioner with a large surgery who was called out to an urgent case, with one patient left in his waiting-room. Before leaving he gave him a hurried examination, and, as he complained of a cough and other typical symptoms, the doctor gave him a quick look and some medicine, and rushed off to his urgent case. One could imagine the feelings of the doctor when, perhaps six or twelve months later, he received a letter from a firm of solicitors stating that their client had been *x*-rayed by a mass radiography unit, that he had been found to have tuberculosis of some months' standing, and that the practitioner had been negligent in his examination. It was a great pity that they could not put over in a court of law the picture of the conditions under which the doctor or perhaps the casualty officer at the hospital had to work. But no doctor liked to say, "As a matter of fact I was in a terrible hurry because I had so many other cases." The mere suggestion of hurry carried with it the implication that he had not paid sufficient attention to the case in question.

Correspondence

Time for Research

Sir,—I am very glad to see that Professor Bryan McFarland (*Journal*, September 17, p. 735) has brought up this important subject. It is no easy matter to discover a good research worker, but, when found, he should be given every encouragement to pursue his bent. At present it means a considerable sacrifice, certainly financially, to begin with, and it may mean, more importantly, losing a chance of promotion at a later date. The Health Service does not appear as yet to give much encouragement to such a man in spite of the proposals suggested in the White Paper on "Clinical Research in Relation to the National Health Service" of 1953 (see *Journal*, July 18, 1953, p. 147). In this there is described the possible career in research, with remuneration, superannuation rights, and promotion, within the National Health Service. Reversion to the service after a certain period of research is then possible, and therefore the advancement of our subject and additional training of the future consultant specialist are achieved. Indeed, such a period spent in research may be regarded as necessary in the training scheme of any specialist or consultant.

Fortunately, the necessities of the situation are appreciated, in Scotland at any rate. It is hoped that regional hospital boards with the support of the Department of Health will collaborate and allow such a surgeon to have some clinical sessions, with an honorary contract of the regional hospital board, and so stay on the roster of the department to which he is attached, thus retaining his salary and status and covering the possibility of litigation. We are fortunate, too, in having in this area the valuable help of a research department of the University in which the research worker is given every help and encouragement. There is no doubt that such a method should be available more widely, and more easily attainable, within the National Health Service.—I am, etc.,

Edinburgh, 3. Walter Mercer.

Gases in Artificial Respiration

Sir,—May this committee avail itself of your columns once more to answer the letter from Dr. H. L. Marriott (*Journal*, March 26, p. 786)? It was felt most important that the committee should have the opportunity of discussing the matter raised, even though this has inevitably caused some delay in the reply.

We believe that two separate questions have arisen in the correspondence, and that they have to some extent become confused. The first question is the resuscitation of patients in respiratory failure requiring artificial respiration. It is only to this matter that our paper refers, and we believe that the evidence (which we need not quote again) is against the use of CO_2/O_2 mixtures in the first-aid treatment of such conditions, in view of the present realization of the dangers of CO_2 excess.

The second question is whether, in the special case of CO poisoning, and when the patient is still breathing spontaneously, the addition of CO_2 to oxygen, by stimulating respiration, increases the rate of excretion of CO, and, if it does so, whether this is important, not merely at once but perhaps in preventing late sequelae of CO poisoning. Here we quite agree with Dr. Marriott that there is need for further experiment, and certain experiments are planned. Without entering again the field of controversy over a difficult and somewhat unconvincing literature, we would at least say that a re-examination of the relevant papers leaves us in doubt as to the soundness of the scientific evidence in favour of this method. We recognize, however, that in certain circumstances physicians in hospital may consider it advantageous to use CO_2/O_2 mixtures. We would again emphasize that the use of such mixtures in the controlled conditions of hospital treatment is very different from their

use as a first-aid treatment for patients who are not breathing spontaneously. The present state of the evidence does not allow us to do more than draw attention to the possible dangers of this method of treatment.—I am, etc.,

BRYAN H. C. MATTHEWS,
Chairman,
Medical Research Council's Committee on Breathing Apparatus for Protection Against Dangerous Fumes and Gases.

London, S.W.1.

Myxoedema

SIR,—With reference to the articles on myxoedema coma by Dr. Marcel Malden and Dr. H. S. Le Marquand and his colleagues (*Journal*, September 24, pp. 764 and 773), and particularly to its occurrence in Hashimoto's disease, by Drs. L. Karhausen and S. Zylberszac (p. 766), it may be of interest to record a further instance.

A widow of 63 was admitted to hospital on October 26, 1954, acutely dyspnoeic. For four months she had lacked energy and had become increasingly short of breath. On examination she was obese, of typical myxoedematous appearance, stuporous, and dyspnoeic. The respiratory movements were very weak and she was cyanosed. There was no oedema or evidence of heart failure. The voice was hoarse and the breathing stridulant. The abdomen was distended and tympanitic. The temperature was 96° F. (35.6° C.)—a special low-recording thermometer was not used. Pulse rate 76 per minute, regular; B.P. 210/110 mm. Hg; respiratory rate 25 per minute. Chest *x*-ray showed a hypertensive cardiac outline with a high diaphragm, and bowel shadows showing between the liver and the right hemidiaphragm. No fluid levels were seen. E.C.G.: Left axis with flattened T waves in all the leads. The only abnormal laboratory finding was a serum cholesterol of 660 mg.%.

Treatment consisted of warming the patient with an electric blanket, and the administration of oxygen and thyroid ¼ gr. (16 mg.) twice a day. However, her temperature remained subnormal (between 96° and 97.4° F. (35.6° and 36.3° C.))—her pulse varied between 70 and 80 per minute, stupor became more pronounced, and the respirations became very poor. She was transferred to an artificial respirator, and given penicillin (1 mega unit twice a day), "eucortone" (20 ml. intravenously), and D.C.A. 20 mg. L-Thyroxine sodium 0.1 mg. twice a day was instituted in place of the thyroid extract. Despite these measures, hypostatic congestion and pneumonia developed, and the patient died on the third day after admission.

At necropsy the thyroid was fibrotic in appearance and weighed 20 g. Colloid-containing thyroid follicles as such were absent, and the remaining individual cells showed bizarre degenerative changes. There was diffuse infiltration with lymphocytes, and broad bands of fibrous tissue were present. The appearances were regarded as those of an advanced stage of Hashimoto's disease. The pituitary weighed 0.75 g. and histologically showed congestion and an increase of acidophil cells. Nothing else of note was found. Although there was no opportunity for radio-iodine studies or investigation of pituitary-adrenal function in this case, it was felt that the clinical appearance, the course of the illness, the hypothermia, slow pulse, respiratory failure, and histological findings combined to confirm a diagnosis of coma and death due to myxoedema.

I am grateful to Dr. W. D. Jeans, consultant physician, for permission to publish these notes, and to Dr. E. M. Stirk for conducting the necropsy and for his opinion on the histology.—I am, etc.,

Leicester. A. W. REID.

SIR,—May I make two comments prompted by recent articles in the *Journal*?

Dr. Marcel Malden is to be congratulated on his interesting article "Hypothermic Coma in Myxoedema," and particularly on his successful treatment of a case with this serious disorder (*Journal*, September 24, p. 764). He refers to evidence for adrenocortical insufficiency in primary myxoedema (a defect perhaps at pituitary-adrenocorticotrophic level, rather than in the adrenal itself). Possibly this is a factor to be reckoned with in severe *non-comatose* cases. Several years ago I saw two such cases deteriorate rather rapidly and die after start of treatment with thyroid. Their behaviour was reminiscent of cases with hypopituitarism given too much thyroid before correction of adrenal insufficiency. Since then I have employed A.C.T.H. as well as thyroid during the initial treatment of severe non-comatose cases of primary myxoedema, and have had no further difficulties. Indeed, the patients have seemed to improve more readily on this combined therapy than on thyroid alone. Long-acting A.C.T.H. has been used in daily doses of 20 units, starting a few days before thyroid and continuing for about a fortnight in all. Whether the deaths or recoveries were *post hoc* or *propter hoc* remains uncertain, but the method of approach is perhaps further trial.

The second comment concerns the histological findings in the case reported by Dr. L. Karhausen and Dr. S. Zylberszac (*Journal*, September 24, p. 766), and presumably in the second case reported by Dr. Malden. The thyroid glands in these two cases were smaller than normal and showed lymphadenoid infiltration. Similar features were present in one of the personally observed fatal cases, referred to above. Lymphadenoid goitre has been thought of as a disorder mainly affecting older women, characterized by goitre and hypothyroidism. Raymond Greene[1,2] has considerably enlarged this conception to include a much wider age group, euthyroid as well as hypothyroid goitrous patients, and an appreciable proportion of patients with thyrotoxicosis. It would appear possible that the disorder may also present as typical primary myxoedema without goitre.—I am, etc.,

London, N.18. D. FERRIMAN.

REFERENCES
1 Greene, R., *J. Endocr.*, 1950, **7**, 1
2 —— Society for Endocrinology, Memoir No. 1, 1953, p. 16.

SIR,—In his medical memorandum (*Journal*, September 24, p. 772), Dr. M. S. Pathy has described an interesting case of myxoedema with serous effusions. Although pericardial effusion in myxoedema is a well-recognized complication, there are some cases of effusions in which clinical manifestations of underlying hypothyroidism are not well developed, especially when seen for the first time. Too much reliance should not be placed on serum cholesterol, which may be normal or may only increase after repeated estimations. Summers,[1] describing myxoedema coma, noted normal figures of serum cholesterol in most of his cases. The E.C.G.s, especially in those few cases with tachycardia due to altered dynamics, may be indistinguishable from other pericardial effusions. Such cases may be wrongly diagnosed as tuberculous, for the aspirated fluid is sterile and may contain high proteins and increased number of lymphocytes. Another point of interest in some cases is the occurrence of pleural effusion or ascites or both together. Marks and Roof,[2] reviewing the literature, quote 13 such out of 25 cases of pericardial effusion.

The exact mechanism of oedema in hypothyroidism is not clearly understood. It could not be due to retention of sodium: Davies *et al.*[3] state that, in spite of decreased glomerular filtration rate, the capacity to excrete salt and water is normal. Capillary permeability has been shown by Lange[4] to increase in myxoedema and recover after administration of thyroid extract in experimental animals.

I suggest that in every case of obscure pericardial effusion, especially in chronic cases with or without fluid in other serous cavities, a possibility of myxoedema should be considered. I wonder whether the estimation of cholesterol content of the aspirated fluid or the examination of crystals microscopically would help in the diagnosis.—I am, etc.,

Manchester, 20. HARI VAISHNAVA.

REFERENCES
1 Summers, V. K., *British Medical Journal*, 1953, **2**, 366.
2 Marks, P. A., and Roof, B. S., *Ann. intern. Med.*, 1953, **39**, 230.
3 Davies, C. E., MacKinnon, J., and Platts, M. M., *British Medical Journal*, 1952, **2**, 595.
4 Lange, K., *Amer. J. med. Sci.*, 1944, **208**, 5.

Position for Delivery

SIR,—In answer to Dr. W. N. Leak (*Journal*, September 17, p. 735) I should like to say that we seem to be the only people in the world who do not use the squatting position for childbirth. I have endless letters from doctors in the East, etc., some even from among the European peasantry.

The result of squatting is that: (1) the force of gravitation is encouraged, not thwarted; (2) the pelvic joints (three) are pulled apart, thus giving more room; (3) the cervix and vagina are connected into one cylindrical passage; (4) the foetal head rests on and pushes past the back of the pubic bone instead of its weight resting on the soft parts and tearing them. And I ask once more, if Newton's tree had been laid on the ground how could the apple have fallen? I think that many congenital eye troubles are due to the enormous pressure and engorgement when the left lateral position is used.

I have used the squatting position successfully in cases in a hospital bed, with the patient's knees on the pillow and her hands on the back rail to steady her and give something to pull on (the old sheet at the bottom of the bed, I imagine, is long superseded, as the pull is all in the wrong direction). If one observes native tribes during defaecation one sees how easy it is in the squatting position; it is the same with parturition—until we interfere and teach the lying-down idea.—I am, etc.,

St. Leonards-on-Sea. KATHLEEN VAUGHAN.

SIR,—I hesitate to argue with Dr. Grantly Dick Read (*Journal*, October 1, p. 850), who has done so much to make midwifery more humane, but when he appeals to the practice of coloured races, saying that it is "the outcome of trial and error for generations past by peoples skilled and experienced in childbirth without association with modern scientific concepts," I think he spoils his case by writing nonsense. Those who have lived among coloured peoples or even studied books about them know that the mystery of sex is where taboos usually hold their strongest sway, and nowhere is the tyranny of the old woman stronger than at childbirth. I should have thought that female circumcision, infibulation, packing the vagina with salt, and similar abominations were supreme examples of the way that fear, ignorance, and immemorial custom constantly lead these people to do things contrary to both nature and health. Whether the results are, as he says, "excellent" depends very much on the shape of the racial head and pelvis, the general physique and absence of rickets, osteomalacia, and so forth. It is impossible to generalize as he does with any safety.

It is true that when a woman drops her baby on the wayside and continues her journey she adopts the squatting position, as does the woman in this country whose baby is born in a chamber utensil. But such cases are not the rule; in fact I had a patient in Kuwait called Nafouda (sand dune) from the unusual circumstance that that was where her mother dropped her. In such cases there is obviously no delay at the outlet, and the squatting position, which has advantages for defaecation, is no obstacle. But when there is any disproportion or difficulty it is far otherwise. Flexing of the thighs does not appreciably pull on the perineum until they reach an angle of about 45°, so that mild bending of the legs does no harm in the majority of cases. But where there is difficulty and the maximum relaxation is required it is given with the legs straight and widely separated.

Where labour is precipitate the woman usually squats, for the abdominal urge is similar to that of defaecation. Where the woman, worn out by the pains of labour, has thrown all instruction and modesty to the winds, or still more when conscious control is removed by partial anaesthesia, in my experience the position she adopts as the head is born is the one I have stated. This is really where one can study uninhibited reflexes and not among coloured races "without association with modern scientific concepts," but hidebound by age-long superstitions and ignorance. Dr. Read asks the curious question whether my patients had had "adequate preparation for labour." I should be sad indeed if anyone thought that these cases bore any relation to my normal midwifery. They are obviously exceptional cases where I was called in late or unexpectedly during the past 40 years, during much of which midwifery was not so well organized as it is now. But the exceptional and regrettable can often throw a vivid light on the more normal and restrained.

As regards the left lateral position, I think the fairly recent correspondence in your columns showed pretty conclusively that where an anaesthetic was given it was much safer than the dorsal. My plea, however, is against the full lithotomy position in normal labour and that where there is delay at the outlet the accoucheur should try the effect of extending and separating the legs. It may not be very convenient for the doctor, but our first duty is to the woman who has trusted herself to our care and to whom an intact perineum is of prime importance.—I am, etc.,

Winsford, Cheshire. W. N. LEAK.

Numbering of Fingers

SIR,—I hope that Dr. Robert Forbes's letter from the Medical Defence Union (*Journal*, October 1, p. 851) will not pass unnoticed. It is, of course, easy in the foot to refer to the great toe, and the second, third, fourth, and fifth toes. Unfortunately, however, the musicians of the world have led us into confusion by indicating finger movement either as x1234 or as 12345. That may be all right for pianists, but it is not all right for surgeons and their assistants who sometimes have to amputate a digit. A year or two ago, after an unfortunate case elsewhere, we agreed at the London Hospital to refer in our notes only to thumb, index finger, middle finger, ring finger, and little finger—and how easy that is, as compared with one, two, three, four, and five.—I am, etc.,

London, W.1. REGINALD WATSON-JONES.

Recurrent Infectious Mononucleosis

SIR,—I was interested to read the report on a case of recurrent infectious mononucleosis by Drs. J. K. Paterson and J. L. Pinniger (*Journal*, August 20, p. 476).

Chronic relapsing infectious mononucleosis was reported in the Middle East in the second world war.[1] Relevant extracts from that paper are as follows: "I have been struck by the relative frequency with which one has elicited a long history indicating that the disease process started months before and was characterized by a short-term febrile phase with sweating, general malaise, aches or pains, and weakness, with or without complaints of sore throat, or painful and tender lymph glands in the neck, etc. These febrile bouts have recurred at intervals and have been given such diagnoses as 'pharyngitis,' 'tonsillitis,' 'P.U.O.,' 'sandfly fever,' 'influenza' or, as happened in the case of a pathologist who subsequently became a colleague of mine, 'atypical relapsing fever'. . . ."—I am, etc.,

Kuala Lumpur, Malaya. JOHN MACKAY-DICK.

REFERENCE

[1] Mackay-Dick, J., *J. roy. Army med. Cps*, 1944, **82**, 279.

Perforation of Intestinal Tuberculous Ulcer

SIR,—The *Journal* of August 6 has just reached here, and I have read with interest the case of a perforated tuberculous ulcer described by Mr. R. G. Talwalkar, of Bombay (p. 362). I am mindful of another somewhat similar case brought to me at my tea-garden central hospital in Assam last year.

A woman aged 26 was admitted in a collapsed condition with abdominal pain and vomiting of eight hours' duration. She gave a vague history of pain in the right iliac fossa for eight days. On examination she looked very ill, emaciated, and anaemic, and the tongue was dirty. The pulse was 110 and of poor volume and the temperature was 99° F. (37.2° C.). The abdomen was tense, tender, and rigid. On vaginal examination she was acutely tender in the right lateral fornix. That an abdominal catastrophe had taken place was evident, and a tentative diagnosis of appendicitis or tubal abscess was made.

She was given intravenous oxytetracycline in a saline drip, and on opening the abdomen a great quantity of watery, purulent fluid welled out. I found a large perforated tuberculous ulcer situated in the small bowel 2 ft. (60 cm.) from the ileo-caecal valve, while half an inch (1.27 cm.) distal to the perforation was an annular constriction almost occluding the bowel lumen. There were numerous tuberculous nodules above and below the perforation. In view of the size of the perforation and of the constriction, 2 ft. (60 cm.) of small bowel was resected and continuity was effected by a side-to-side anastomosis. The patient made an uninterrupted recovery. Detailed examination of the resected specimen suggested that the constriction was due to an old healed tuberculous lesion.—I am, etc.,

Jalpaiguri, India. W. D. V. Burton.

Overdose of Reserpine

Sir,—A girl aged 1 year and 6 months was admitted to the Children's Hospital, Colombo, on May 20, 1955, with the following history. Her grandfather had been discharged from hospital the previous day with a box of 30 tablets (0.25 mg. each) of "serpasil" (reserpine). He had taken only one of these tablets after coming home. At 4.30 p.m. on the day of admission the child's mother found the child eating tablets from this box, and there were only four left. Thus 25 tablets had probably been taken. The child vomited twice half an hour later. She was then brought to the out-patients department at 6 p.m., where she vomited again (twice). There was increasing drowsiness from the time when the tablets were taken.

On admission to the ward, the child was found to be extremely drowsy. The pulse was just perceptible. No abnormalities were detected in the heart, lungs, or abdomen. The blood pressure was 50 mm. systolic, and 20 mm. diastolic. The stomach was washed out and an intramuscular injection of ephedrine ¼ gr. (16 mg.) given. There was no change in the child's general condition in the night. The next morning she was less drowsy, her face was flushed and somewhat swollen, and the blood pressure was 100 mm. systolic and 50 mm. diastolic. On the parents' insistence she was discharged. The child was seen again on July 8. No abnormalities were discovered in the heart, lungs, or abdomen. The blood pressure was 90 mm. systolic and 50 mm. diastolic. The parents said that the child was drowsy and flushed for two days after discharge from hospital.

In the 2½ hours that had elapsed between the time that the tablets had been swallowed and the time of the admission the child had vomited four times. Thus it is probable that most of the drug ingested had been got rid of. However, a fair amount must have been absorbed, as shown by the drowsiness and fall of blood pressure. One of the patients treated by Vakil[1] accidentally received ten times the dose of reserpine tablets—that is, 20 tablets—which caused no more inconvenience than a feeling of lassitude and giddiness, lasting for two days. It is interesting to note that the case reported was drowsy and flushed in the face for two days.—I am, etc.,

Colombo. Trevor Phillips.

Reference

[1] Vakil, R. J., *J. Indian med. Ass.*, 1953, **23**, 97.

Prolonged Pregnancy

Sir,—In Mr. George B. Gibson's admirable article on prolonged pregnancy (*Journal*, September 17, p. 715) he states that he would, in those cases showing lack of effacement of the cervix and an unfixed foetal head, perform a membrane sweep and give a hot vaginal douche. This is surely a contradiction of his advocacy of "masterly inactivity" until labour starts spontaneously, particularly when one remembers the small but appreciable incidence of sepsis following a procedure which, by itself, has been shown to be of little effect in the induction of labour.—I am, etc.,

Wuppertal, Germany. J. B. Pearson.

Carcinogen in Coal-tar

Sir,—Surely Sir Ernest Kennaway (*Journal*, September 24, p. 749), in his brilliant study of the isolation of the active carcinogenic substances from pitch, has pointed to the major cause of cancer of the lung. He first makes the point that heating relatively simple hydrocarbons to a high temperature—such as that of the fusion of glass—induces polymerization and the formations of carcinogens in an inert atmosphere. These conditions, I submit, are ideally reproduced in compression ignition engines; it is well known that in the cylinders both of compression ignition and internal combustion engines combustion is only partial. The mixture of gases within the cylinders of the former, for a variety of reasons, can be considered comparable with the hydrogen atmosphere conducive to polymerization. Only in compression ignition engines is the heat engendered by gaseous compression sufficient to fire the gases—that is, comparable with the heat of fusion of glass. Thus, at the very least, a strong case can be made out that the exhaust from diesel engines is specifically carcinogenic.

But Sir Ernest goes on to tell us that it is simple to detect carcinogenic substances; for both by the absorption spectrum method and by ultimate testing with sulphuric acid it is possible to test the cancer-producing virulence of the effluvium from diesel engines. Surely this is a very proper field for research for that torpid body, the Road Research Laboratory. Diesel oil itself is a mixture of aromatic hydrocarbons, relatively simple in structure, with the same basic structure of the benzene ring as tar or pitch, but should be even more readily productive of carcinogenic substances than tar or pitch if only for the fact that the liquid fuel should be easily polymerized to four or five rings of dibenzanthracene, benzpyrene, or methyl cholanthrene. Now Sir Ernest mentions that 1:2:5:6:-dibenzanthracene is carcinogenic in a dilution of 0.003% in benzene, which is 30 parts per million. But this is in solution. What then is the minimum strength required of a carcinogen which is volatilized by heat, then diffused into the atmosphere, and necessarily inhaled by all and sundry? Surely the carcinogenic substances would reach the lung alveoli in intimate contact and in ample concentration to do their deadly work. A further important point in this connexion is that so very many diesel lorries have defective fuel injector pumps, which cause the discharge of a thick black fog of exhaust gases with a probable tenfold concentration of carcinogenic hydrocarbons. If this were so—and Sir Ernest's article suggests that this can readily be decided—a terrifying prospect opens up.

Assuming this to be so, there would be two factors in the production of cancer of the lung: (1) concentration of carcinogen and (2) period of contact. A heavy concentration of carcinogen would need but a short period of contact, and vice versa. When I qualified in 1929 cancer of the lung was virtually unknown. Yet smoking as a national male habit had been prevalent for some 20 years. Diesel engines began to displace petrol engines in the early 'thirties in lorries, and have grown in numbers in almost geometric ratio since. When going through the town of Chester this summer I was struck not only by the extreme density of traffic but particularly by the stench of diesel exhaust gases, which was uniform all over the city. This theory of lung-cancer formation would account, moreover, for the disparity in figures of deaths from this cause between town and country: there would naturally be a preponderance of deaths in towns. Diesel oil itself is a mixture of aromatic hydrocarbons, relatively simple in structure, based on benzene rings or aggregates of benzene rings as are tar and pitch, but should be more readily productive of carcinogenic substances than the latter, if only because the vaporized liquid fuel should polymerize more easily at the temperature of compression ignition to the four rings of dibenzanthracene or benzpyrene, or to the five of methylcholanthrene, than could the more solid aggregates of tar or pitch. Indeed, the recent paper by Clemo *et al.*[1] suggests that both industrial smoke as well as diesel oil exhaust may stimulate the

production of lung nodules in mice: and Waller[2] has detected 3:4-benzpyrene in the deposit of the exhaust of diesel compressors.

While I would be the last to contest the validity of the statistics of Doll and Bradford Hill, there is no doubt at all that the curve of deaths from carcinoma of the lung follows a little later, but closely parallel with, the curve of vehicle density of diesel lorries. This theory should be tested immediately; and if the diesel exhaust is carcinogenic then it behoves the Government to sponsor research by active bodies; for if it is so, then the constantly increasing number of lorries on the road promises to give us such a crop of lung cancers in the next decade as we doctors have never yet dreamed of.—I am, etc.,

Rothwell Haigh, Yorks. C. E. GOLDSBOROUGH.

REFERENCES

[1] Clemo, G. R., Miller, E. W., and Pybus, F. C., *Brit. J. Cancer*, 1955, 9, 137.
[2] Waller, R. E., ibid., 1952, 6, 8.

Neurosis in General Practice

SIR,—With reference to Dr. J. Fry's comments on the incidence neuroses in general practice (*Journal*, October 1, p. 853), the following might be of interest.

I had previously accepted the estimates of 30% and higher quoted by Dr. J. C. E. Pougher (*Journal*, August 13, p. 409), and, with the intention of proving this to be true, I have recorded all items of service rendered over a period of twelve months, and hope to classify them to show what part of the general practitioner's work is due to neurosis, psychosomatic disorder, and to psychosis. Restricting neurosis to mean conversion hysteria, anxiety neurosis in all its forms, and obsessive-compulsive reactions, it was surprising to find that of just over 10,000 items, only 700 were due to neuroses.

It is possible that the figure will approach 30% when psychosomatic disorders are added, but I am convinced that the incidence of pure neurosis in general practice has been greatly overestimated. A patient is not neurotic because he attends with what seems to the doctor a trivial complaint. He is no more so than the stoic who works on through illness and does not seek help because of a different psychological make-up.—I am, etc.,

Dundee. RONALD A. B. RORIE.

"Roter" Tablets

SIR,—Dr. Roderick R. Hamilton is to be congratulated on his article "Treatment of Peptic Ulcers with 'Roter' Tablets" (*Journal*, October 1, p. 827).

I note that "the patients were instructed to take two tablets three times a day after food for three weeks." Generally this "after food" business means, to the patient, immediately after food. As the stomach contents are alkaline after a meal, extra alkalis would appear to be uncalled for. Indeed, the extra alkalinity will necessitate increased acid production, since food is not digested until definitely acid in reaction. Surely, then, roter tablets, or other alkalis, should only be administered if there is an *excess* of acid, in, say, half an hour to an hour after a meal, and not even then if the patient does not have the symptoms of hyperacidity.—I am, etc.,

Currie, Midlothian. H. MAITLAND MOIR.

Fluoridation of Water

SIR,—I would like to join with Dr. William C. Fothergill (*Journal*, September 24, p. 791) in his resentment against the mass fluoridation of a population of any size—let alone one such as Darlington's. It may be salubrious to reflect that the dye industry began with a 13- or 14-year-old experiment in Germany, which, in trying to synthesize quinine, made a dye "mauvine" in the last century. This proved the precursor of the aniline dye industry, but it was nearly 50 years later that the lethal carcinogenic properties of β-naphthylamine were proved. The chemical industry is well aware nowadays of the possibility of toxicity of new compounds.

In spite of every kind of precaution taken by research, animal experiment, and so on, there can never be any certainty of the human reaction to a new molecule for at least one generation. Let us admit that we live in a dangerous age, but let us not add to our dangers by forcing people to consume fluorides—or any other substance—when their toxic properties are already known, and, as Dr. Fothergill so eloquently puts it, in quantities which are uncontrollable.—I am, etc.,

Wrexham. R. P. W. KUP.

Treatment of Simple Rib Fracture

SIR,—The method of treatment of simple rib fracture described by Mr. H. D. W. Powell (*Journal*, October 1, p. 829) may prove of great practical interest to those of us in general practice who have found the strapping method unsatisfactory for the relief of pain. Unfortunately I cannot agree with his conclusion that this method could be used prior to *x*-ray examination. In present-day practice most would agree that to treat a suspected fracture of rib without *x*-ray, even if of no practical use in itself, is heading for trouble. A patient expects to be *x*-rayed, and the fear of litigation compels a cautious practitioner to cover himself by having this done before contemplating local injection at the site.—I am, etc.,

Hull. MICHAEL S. SANDERS.

Exophthalmos

SIR,—I see that in your annotation on exophthalmos (*Journal*, September 10, p. 667) it is stated that the secretion of an exophthalmos-producing factor has not yet been either proved or disproved. Is the writer unversed with the work of Brown M. Dobyns, of Cleveland? He should read Dobyns's paper.[1] If he finds this work unconvincing, he might at least have referred to it.—I am, etc.,

Sheffield, 10. B. N. CATCHPOLE.

REFERENCE

[1] Dobyns, B. M., and Wilson, L. A., *J. clin. Endocr.*, 1954, 14, 1393.

A Simple Blood-grouping Method

SIR,—Attention has been drawn by Mr. J. T. Rice-Edwards (*Journal*, September 10, p. 681) and others to a method of blood-grouping using cards impregnated with different blood-grouping sera. There are two major objections to this alleged simple method.

First, no blood-grouping can be considered safe which relies solely upon cell grouping and does not allow of the safeguard of checking the serum of the person to be grouped against known A and B cells. The absence of controls on the card system makes this omission the more important. Obviously, this serum check cannot be done on any form of dried material. Secondly, blood-grouping serum dried on to cards has a very limited life owing to denaturation of the proteins carrying the antibodies. This gives rise to equivocal readings after a variable interval and ultimately to complete absence of agglutination, so that all the tests would appear negative.

Some years ago workers in the Blood Transfusion Laboratory at Montpellier produced what was called a *hémobiotest rapide*, which consisted of a card carrying panels of dried anti-A, anti-B, and anti-AB and anti-Rh (D) sera. These panels were protected by a loose "cellophane" cover. After quite a short time, under normal conditions of storage at room temperature, the sera became inert and gave negative readings with A and B and with Rh-positive cells. Apart from failure of the primary object, that of grouping the blood under test, there is always the danger that the holder of such a card may be used as a blood donor. The result of this may well be disastrous, since the inactive sera will suggest that he is group O Rh-negative.

Finally, it is not easy to understand Dr. Philip Boyd's difficulty (*Journal*, September 24, p. 793) in obtaining ordinary grouping sera for use in his laboratory. I take it he has made application to his local blood transfusion

centre. I feel sure they would either group his employees or provide the necessary serum rather than encourage him to use a method which is unsafe, apart from being quite costly.—I am, etc.,

Sutton, Surrey. R. A. ZEITLIN.

Animals in Research

SIR,—I should like permission to express my wholehearted support for your correspondents Dr. G. L. Davies (*Journal*, August 6, p. 378) and Dr. G. Whitwell (*Journal*, September 10, p. 681). Experiments on animals have become so dominant a cult that in our teaching schools nothing in medicine or surgery is accepted unless it has been "confirmed" by animal experiments even though the facts have been established for many years—unless of course it is expedient not to accept the confirmations (*vide* Semmelweis). Apart from the brutal type of physiological experiments, such as drowning experiments with 160 dogs, which Dr. K. W. Donald (*Journal*, July 16, p. 155) found "particularly interesting," standardization of drugs and physicists' accurate scientific measurements of irradiation fail to give the practitioner the slightest indication of the most variable factor—the response of the patient. Consequently he may lose his patient with a standard dose. Medicine is an art and not a science, and I believe that the patient is far safer in the hands of the practitioner who administers his treatments cautiously, but empirically, than in the hands of one who administers the most accurately determined scientific dose which the vivisectionists have supplied.

I note that you, Sir, head the correspondence column with this note: "*Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.*" In view of this, can the publication on "Drowning," containing so many thousand words and occupying so many pages, be justified? Is not the essential gist of it already well known to all practitioners? It is to be found in the handbooks on first-aid for novices. I have one before me which bears it in block letters: "Artificial respiration must begin immediately. The assistants must be warned that their actions must, on no account, interfere with artificial respiration." Surely only a consultant would attempt to stop it to examine the patient.—I am, etc.,

Birmingham, 15. JAMES F. BRAILSFORD.

SIR,—Your correspondent Dr. W. Lane-Petter (*Journal*, September 24, p. 788) evidently believes there may be a way of more or less drowning and reviving animals which is not cruel. We would be glad to know more about it. He would hesitate to suppose any experimenter capable of cruelty, but he says that, on occasion, they cause severe suffering. I find that rather odd.—I am, etc.,

Manchester, 14. J. L. DOBBIE.

Contraindications to Thiopentone Anaesthesia

SIR,—The leading article (*Journal*, October 1, p. 836) on contraindications to thiopentone anaesthesia will be welcomed by every anaesthetist. It gives a timely reminder of the potential dangers of this anaesthetic. In the hands of the inexperienced thiopentone may become a lethal weapon, and this has already been the subject of legal comment.[1]

Many of these dangers are, however, avoidable if soluble hexobarbitone is used instead of thiopentone. It is unfortunate that the greater safety of this drug was lost sight of with the introduction of the much more potent drug thiopentone. No case of gangrene following intra-arterial injection of soluble hexobarbitone has ever been reported, while perivenous injection does not produce a slough. Recent work by Mayrhofer[2] has shown that bronchial spasm is four times more common with thiopentone than with hexobarbitone.

In the past there have been objections to the use of hexobarbitone on the grounds that it did not produce sufficient depth of anaesthesia, but with the almost universal use of muscle relaxants these objections are no longer valid. Indeed, the combination of hexobarbitone and a muscle relaxant produces a much smoother anaesthesia.

Lastly, but by no means least, the teaching of anaesthesia to students and newly qualified housemen is a much safer procedure where hexobarbitone is the intravenous drug used, and not thiopentone.—I am, etc.,

London, W.1 MASSEY DAWKINS.

REFERENCES

1 *British Medical Journal*, 1951, **2**, 422.
2 Mayrhofer, O., *Der Anaesthetist*, 1954, **3**, 105.

SIR,—Your leading article on thiopentone (*Journal*, October 1, p. 836) would seem to call for comment in several respects. In particular, the advocacy of thiopentone followed by succinylcholine, and intubation with a cuffed endotracheal tube for cases of intestinal obstruction and possibly for obstetric cases, must not be allowed to pass without qualification.

The passage of a stomach tube cannot with certainty ensure the complete evacuation of the contents of that organ, especially as the tube is frequently of the Ryle's type and not full size. In addition, the tube is not infrequently found coiled in the pharynx, when a reassuringly dry aspiration will be obtained. Under these circumstances succinylcholine should never be used as a relaxant for intubation without first ensuring a head-up tilt of at least 20 degrees. This avoids the possibility of passive regurgitation of gastric contents as the relaxant takes effect, a danger which is very real and once happened to the writer, fortunately without grave result. In obstetrical work it is not usually practicable or expedient to pass a stomach tube, although a full stomach is not unlikely. In addition, the operating table, especially during forceps deliveries, is frequently incapable of adjustment. Under these circumstances, therefore, the use of succinylcholine as a relaxant would seem inadvisable, and a more simple technique of nitrous oxide, oxygen, and trichlorethylene or ether would be more suitable.

The dangers of tissue necrosis and gangrene associated with the use of thiopentone can be very largely abolished by using for venepuncture a vein on the dorsum of the hand in preference to one in the cubital fossa. Although it is more painful than in the latter position, intra-arterial injection is impossible and the local swelling of extravenous injection is immediately apparent before more than a few minims have been used. After a little practice venepuncture in this locality will very frequently be found easier than in the cubital fossa, especially in obese patients, provided sufficient time is given for the veins to become distended.

Finally, the avoidance of giving repeated doses of thiopentone with its cumulative action over several days has been emphasized by Dundee,[1] whilst Pender[2] has shown that patients undergoing cortisone therapy react badly to both barbiturates and opiates.—I am, etc.,

Edgware, Middlesex. A. VIVIAN JENKINS.

REFERENCES

1 Dundee, J. W., *Anaesthesia*, 1955, **10**, 139.
2 Pender, J. W., *Wis. med. J.*, 1954, **53**, 215.

SIR,—In the leading article (*Journal*, October 1, p. 836) on contraindications to thiopentone anaesthesia it is suggested that in cases of intestinal obstruction the stomach should be evacuated, and then induction of anaesthesia with thiopentone and succinylcholine should be followed by immediate insertion of a cuffed endotracheal tube. I think that this description needs amplifying.

It is seldom possible to be absolutely certain that the stomach has been successfully evacuated, and, if not, regurgitation may occur with the above technique, *if the patient is in the horizontal position*. It has been suggested that this may be prevented by using a foot-down tilt of at least 20 degrees.[1] This tilt should be mentioned again if the same technique is to be advocated in obstetrics.

Finally, I think it is true to say that it is not yet generally agreed amongst anaesthetists that this technique is the safest in the conditions described. Many prefer to avoid thiopentone and the muscle-relaxants for induction, and, following evacuation of the stomach, induce anaesthesia with the nitrous-oxide–oxygen–ether sequence before inserting a cuffed endotracheal tube.—I am, etc.,

London, E.C.1. ROBERT I. W. BALLANTINE.

REFERENCE

[1] Morton, H. J. V., and Wylie, W. D., *Anaesthesia*, 1951, **6**, 190.

SIR,—Your leading article (*Journal*, October 1, p. 836) on the contraindications to thiopentone anaesthesia, both prudent and wise, raises two questions: (1) What are the indications for the use of thiopentone when hexobarbitone is available? (2) What are the indications for the use of a 5% solution of thiopentone?

Hexobarbitone does not cause respiratory arrest as thiopentone does; it does not damage the tissues; I know of no record of it causing harm when given intra-arterially; it does not depress the infant's respiration when used in obstetric anaesthesia. As regards 5% solutions of thiopentone, this malignant concentration has no known advantage over the bland 2½% solution now in general use, but has many disadvantages which you stress. If hexobarbitone is not available I use a 2½% solution of thiopentone.—I am, etc.,

Gloucester. J. SHEGOG RUDDELL.

The Painful Heel

SIR,—I was interested to read Mr. G. K. Rose's article on the painful heel (*Journal*, October 1, p. 831). Like most orthopaedic surgeons, I too have found this condition difficult to treat effectively.

I would like to ask Mr. Rose to try a local injection of hydrocortisone on some of his cases of calcaneal spur with pain. In a small number of cases—too small to be statistically significant, I must admit—I have found this drug very effective.—I am, etc.,

Colne, Lancs. DAVID A. RICHMOND.

Intersexuality

SIR,—Mr. L. R. Broster pays a gracious compliment in his comment (*Journal*, October 1, 849) on the papers by Dr. C. N. Armstrong (*Journal*, May 14, p. 1173) and myself (*Journal*, September 17, p. 709). I agree with him that it would have been most interesting to study the histology of the gonads (I do not think they should be called "ovaries") of these patients, but I doubt whether it would have been clinically justifiable to have subjected the patients to laparotomy solely for this purpose. As I mentioned in the addendum to my paper, Greenblatt and Carmona[1] have described what must be a similar case to my own; they found the gonads to be rudimentary and to consist of a cortex composed of stroma without follicles, and a medulla and hilus containing many "Leydig cells." This condition of course resembles that found in the gonadal agenesis (or Turner's) syndrome, many examples of which are now known to be of male chromosomal sex.

The question of the "chromosomal" sex in so-called true hermaphrodites, which Mr. Broster raises, is clearly a fascinating one. On theoretical grounds, it would be reasonable to assume that such individuals must have at least the XX chromosomal constitution, and would therefore appear to be "female" by the nuclear sexing techniques (skin biopsy, polymorphonuclear leucocytes, buccal scrapings) now being used. Some, at least, of the true hermaphrodites appear to have the XXY constitution which would also be interpreted as "female" by the above techniques. If they mean anything, such techniques should imply absence of the XX constitution when they indicate the "male" sex, and I would therefore think it justifiable to conclude that both my patients were XY in respect to their sex chromosomes. Perhaps I may be permitted to add that both patients have now had several oestrogen withdrawal bleedings.—I am, etc.,

London, N.W.1. G. I. M. SWYER.

REFERENCE

[1] Greenblatt, R. B., and Carmona, N., *J. clin. Endocr.*, 1955, **15**, 877.

The Whitfield Tradition of Therapy

SIR,—Dr. David I. Williams, with courteous alacrity, has given us (*Journal*, October 1, p. 850) the source of his "original formula" for Whitfield's ointment. Is it not time Drs. J. E. M. Wigley and F. B. Fox came clean? The carefree agricultural confusion in my letter (*Journal*, September 17, p. 737) was due to the deletion (with my approval) of the central paragraph referring to a rapture of errors in Dr. Williams's article. We Chellinham yokels are delighted that Camberwell is still interested in topics rural. News has reached us that it has lost its butterfly.—I am, etc.,

Cheltenham. G. B. MATTHEWS.

Penicillin Anaphylactoid Shock

SIR,—Dr. T. H. Tidswell's account of cases of penicillin shock treated with adrenaline (*Journal*, September 17, p. 721) is very interesting, and has provoked me to mention a recent case of mine treated most satisfactorily otherwise.

A healthy man aged 65 years attended the casualty department on September 15 with threatening cellulitis of his face, developing from a septic spot on the upper lip. He was given an injection of one mega unit of crystalline penicillin in the deltoid muscle. Within a few seconds he complained of extreme dizziness and choking. He started to perspire heavily, went pale and cyanotic and dyspnoeic, with markedly laboured and wheezing respiration. In another two minutes he became unconscious, cold, and flaccid, with subnormal temperature. Pulse was very soft and 104/min. and blood pressure 90/40 mm. Hg. His face, eyelids, and forehead were swollen, and eyes congested and running. There were wheezing rhonchi all over the lungs on auscultation.

He was immediately given an intravenous injection of 10 ml. of aminophylline (theophylline with ethylenediamine 4 gr. (0.25 g.) in 10 ml.), followed in five minutes by an intramuscular injection of antazoline 2 ml. (0.1 g.). His general condition improved very quickly, and in a few minutes his breathing became easy, colour improved, and sweating diminished. Within the next half-hour he was restored to almost normal condition and blood pressure went up to 120/80 mm. Hg.

The same penicillin was being given by injection to other patients without any after-effects.

In elderly people of this age or more, and specially where the cardiovascular condition is unknown and final diagnosis is somewhat doubtful, management of this type of shock by aminophylline is, in my opinion, comparatively safe and preferable.—I am, etc.,

Southport. B. BHATTACHARYA.

St. Luke's Day

SIR,—October 18 comes to remind us of the patron saint of our profession, and our indebtedness to him. His fame rests not so much on his work as a medical man as on his writings. Luke was, perhaps, the writer who, by his writings, has influenced the mind of the world more for good than any other. He is a literary artist, and he has left us a most beautiful and attractive picture of the greatest of all psychiatrists and physicians.

Luke has also left us a second great literary work—"Acts of Apostles." Do we realize that this second treatise of Luke describes the birth of the first international society for the betterment of the world? It was indeed the first of all international societies. Luke's service to the world in leaving us these painstaking histories of the birth of Christendom is incalculable. We may well use the prescriptions they contain for the diseases of our souls. Has any other remedy ever been found that is more effective in curing us of selfishness and materialism?—I am, etc.,

Banstead, Surrey. HERBERT CAIGER.

Obituary

T. J. MACKIE, C.B.E., M.D., LL.D., M.R.C.P.Ed.

Professor T. J. Mackie, professor of bacteriology and dean of the Faculty of Medicine in the University of Edinburgh, died suddenly at his home in Edinburgh on October 6 at the age of 67. Earlier in the evening he had presided at the inaugural address given by the professor of psychiatry.

Thomas Jones Mackie was born at Hamilton on June 5, 1888. He was educated at Hamilton Academy and Glasgow University, where he graduated M.B., Ch.B. with honours in 1910, gaining the Brunton Memorial Prize as the most distinguished student of his year. After house-surgeon and house-physician appointments in Glasgow Western Infirmary he proceeded to a Carnegie Scholarship in the department of pathology, attracted to the laboratory by Professor (now Sir Robert) Muir. There he came under the influence of C. H. Browning, later to be professor of bacteriology in Glasgow, and had as contemporaries that remarkable group of young men who were ultimately to fill such a high proportion of the professorial chairs of pathology and bacteriology in Britain. In 1913 he took the Oxford D.P.H., and was working as an assistant in the Bland-Sutton Institute of Pathology at the Middlesex Hospital when, as a Territorial, he was embodied as an officer in the R.A.M.C. at the outbreak of war in 1914. He served mainly in the Middle East, where his special experience of the coli and cholera organisms was of the greatest value. This stimulating environment helped to shape Mackie's future career. Though young in years, he was appointed to command the Central Bacteriological Laboratory in Alexandria, and his distinguished record there led to his appointment in 1918 to the Werner-Beit chair of bacteriology in Capetown University. This new department provided ample opportunity for Mackie's organizing ability. In 1923, on the retirement of Professor Ritchie, Mackie was invited to the chair of bacteriology in the University of Edinburgh.

Mackie came to Edinburgh at the age of 35 with a brilliant reputation as a bacteriologist, an investigator of originality, a personality abounding in energy. It is not surprising that his department became a centre of activity. He once epitomized his policy: Choose the best men, equip them generously, and give them their heads. The results speak for themselves. In the course of the 32 years of Mackie's tenure of the chair a notable number of men trained by him were appointed to senior bacteriological posts at home and abroad. Five of his pupils adorn chairs of bacteriology, and many who worked with him have attained distinction in other fields of medicine and surgery. All who came under his influence have spoken of his remarkable grasp of his immense subject and of its relationship to the sister sciences.

Characteristically, his department at Edinburgh was probably the first in the country to enlist a biochemist for bacteriological problems. He was quick to encourage virus studies, and under his guidance Rhodes, Van Rooyen, and Swain, among others, have made notable contributions. His remarkable energy was exemplified in his joint authorship of two standard and popular textbooks: with C. H. Browning he wrote a *Textbook of Bacteriology* (formerly Muir and Ritchie's *Manual of Bacteriology*), the eleventh edition of which appeared in 1949, and with J. E. McCartney *A Handbook of Bacteriology*.

Professor Mackie's personal researches covered a wide range of subjects. In Muir's laboratory his early work was immunological and was concerned with the nature of complement and its fractionation. Immunity always held a special fascination for him. He classified the coli-dysentery group of bacilli. The *Spirillum minus* of rat-bite fever interested him, and he was one of the first to recognize the virus nature of louping ill of sheep. He was a pioneer in the application of the Sachs–Georgi reaction to the diagnosis of syphilis. His researches on tetanus assumed special significance with his demonstration of surgical catgut as a source of the infection—a discovery which under his stimulus led to the appropriate amendment of the Therapeutic Substances Act. Veterinary and agricultural bacteriology occupied most of his time, and his influence, direct and indirect, stimulated an immense volume of fundamental and applied research in these wide fields.

Professor Mackie was greatly in demand as counsellor and adviser to many bodies, professional and lay. He was honorary bacteriologist and senior consultant in bacteriology to the Royal Infirmary of Edinburgh, and until a few years ago a member of its board of management. For some time he served on the South-eastern Regional Hospital Board, to which he was adviser, and he was also a member of the council of the Lister Institute of Preventive Medicine. A former member of the Scientific Advisory Committee of the Department of Health for Scotland, he was chairman of the Infectious Diseases Subcommittee. In the second world war, as in the first, he gave generously of his resources. He was closely associated with the development of the laboratory service in Scotland, and at the beginning of the war housed the Central Military Laboratory in his own department. In the field of agriculture he served on the Agricultural Research Council, was a director of the Animal Diseases Research Association (Scotland), and was chairman of the Scottish Hill Farm Research Committee. To these committees he gave his knowledge and enthusiasm. He felt it was time well spent, and often confessed to the pleasure of departmental excursions to the Scottish hills. He was appointed C.B.E. in 1942, and in 1947 Glasgow University conferred on him an honorary degree of Doctor of Laws. He was a Corresponding Member of the Academy of Medicine of Rome, a Member of the Royal College of Physicians of Edinburgh, and a Fellow of the Royal Society of Edinburgh. During the course of his career he had been an examiner at one time or another for the universities of Aberdeen, St. Andrews, Glasgow, Durham, and Sheffield. He was twice vice-president of the Section of Pathology and Bacteriology at Annual Meetings of the B.M.A.

G. L. M. writes: By the death of Professor T. J. Mackie, Edinburgh University and Scottish medicine have sustained a grievous loss. Nurtured in the Scottish universities, he believed passionately in their contribution to scientific medicine. He was a jealous guardian of their traditions, a champion of their welfare. His long experience of university matters at all levels gave him a unique position in the medical school of Edinburgh University.

Assistant to the dean for many years, Mackie succeeded Sir Sydney Smith as dean of the Faculty of Medicine in 1953. He was a member of the University Court and a Curator of Patronage of many members. To-day it is sometimes deplored that acknowledged experts in their subjects should in later years devote much of their time and energy

to administration. Professor Mackie's record casts doubts on the correctness of this point of view. It was impossible to separate his professional status and administrative ability; his opinion commanded respect as much for his scientific distinction as for his statesmanship. The truth is that, with the complexities of university expansion in the post-war years and with the establishment of the National Health Service and its repercussion on university life, the services of a man of Mackie's calibre were invaluable, and we can acknowledge them with thankfulness. He would have been the last to deny that he enjoyed it all, though from time to time many of us felt that the strain was too much and urged him to rest. Indeed, he had planned to resign some of his administrative duties in the near future, but it is difficult to imagine that vital personality becoming progressively less active.

"T. J." will be greatly missed. His sudden death has shocked his colleagues and friends: he was a man of such energy and activity that it was difficult to remember he had been gravely ill a few years ago. His sense of occasion graced all his official duties, social and administrative. In private he was the most engaging companion, enjoying to the full the anecdotes, always kindly and told with infectious mirth, from his rich store of experience of men and affairs. Few men can have drawn more affection from colleagues and staff, none could have been less conscious of it. He had the great virtues of integrity and courage, of kindliness and consideration for others. The students have lost a friend; they can never know his devotion to their interests and his concern for the welfare of the individual. He died on duty as he would have wished; his memorial is the great medical school he loved so well.

Professor Mackie is survived by a widow, by a son who is a political officer in West Africa, and by a daughter who is engaged in gynaecological practice in Edinburgh.

DAVID CHEEVER, M.D., F.A.C.S.

We record with regret the death of Dr. David Cheever, surgeon emeritus at the Peter Bent Brigham Hospital, Boston, U.S.A., and formerly professor of surgery at Harvard University.

David Cheever, who was born in Boston in 1876, came of a well-known Boston medical family. He graduated M.D. at Harvard in 1901 and after an internship at the Boston City Hospital was appointed to the surgical staff of that hospital and later to the Peter Bent Brigham Hospital. He also became associate professor in surgery at Harvard. In 1940–1 he was president of the American Surgical Association, and a year later was elected an honorary fellow of the Royal Society of Medicine.

Mr. L. R. Broster writes: In the medical annals of Anglo-American friendship the name of David Cheever will always hold a high place, for as a surgeon, a teacher, and a writer he was of the same mould as Osler. A graduate of Harvard, he held successively from 1913 the posts of assistant, associate professor, and full professor of surgery in that university, with a long record in the teaching of anatomy. He was also surgeon to the Boston City Hospital (1905–12) and to the Peter Bent Brigham Hospital (1913–42).

During the first world war he served with the rank of lieutenant-colonel in the British Expeditionary Force. He was chief surgeon to No. 22 Base Hospital and in charge of the Harvard Unit (1915–16). After 1939 he became an overseer of Harvard University, and among his many honours was that of president of the Boston Medical Library.

Cheever was one of those men to whom an active surgical career brought a broad-minded philosophy of life. His publications on general surgery ranged over a wide and varied field, but, gifted with a lucid mind, a fluent pen, and a fine and cultured literary style, he was able to write successfully on such subjects as history, education, ethics, and on professional matters relating to the general public.

I came to know Cheever in 1941, when invited by the American Surgical Association to talk on "War Surgery," and was one of those privileged to listen to his presidential address, "Mars and Aesculapius," delivered at White Sulphur Springs. From Homer onwards he marshalled the historical facts of medicine in relation to war, and referred to "the magical transformation of pest houses into hospitals" by Florence Nightingale as "one of the most stirring epics of our race." He was proud of his Cambridgeshire heritage, whence his forebears emigrated to New England in the seventeenth century. The concluding remarks of his address were as stirring in their concern for Britain as they were prophetic of America's entry into, and the outcome of, the war.

In 1942 Cheever was elected an honorary fellow of the Royal Society of Medicine, a distinction he particularly appreciated, because it enabled him to follow with pride and interest the career of his protégé and successor, the late Dr. Elliott Cutler, chief surgeon to the American Forces in England, who, with General Paul Hawley, did so much to help in organizing the Interallied Conferences on War Medicine sponsored by the Society.

Cheever was a warm-hearted friend and an ideal correspondent. His long, forthright, and penetrating letters on diverse subjects, written in immaculate longhand in spite of increasingly painful and crippling arthritis, were a pleasure and an inspiration to read. He was most regretful recently that his declining health made it impossible for him to see some of his old friends who were visiting Canada and the U.S.A.

Dr. G. H. Peake died at Guildford, Surrey, on September 21 at the age of 84. George Henry Peake was born in Madagascar on December 13, 1870, the son of the Rev. P. G. Peake, and received his medical training at Edinburgh, taking the Scottish triple qualification in 1892. He then joined the London Missionary Society and went to Madagascar as a medical missionary. After some years there he came back to the United Kingdom for a well-earned rest, and during that period obtained the F.R.C.S.Ed. in 1903. Returning to Madagascar, he continued his Christian work there until 1909, when ill-health forced him to come home for good. Until recently many of his old patients among the islanders had continued to write to him. He was in practice at Parkstone, Dorset, when the first world war broke out in 1914. Commissioned as a major in the R.A.M.C., he served with a unit of the British Red Cross Society, first in a Belgian field hospital, and later in a hospital at Lyons. After the war he practised at Guildford, and took an active part in the work of the St. John Ambulance Association. In 1938 he retired from general practice, but during the second world war he acted as chairman of the Ministry of Pensions medical board at Guildford. Of a kindly disposition, Dr. Peake made many friends during his long life, not least among his patients. His wife, the daughter of the Rev. J. Frédoux, was a niece of Dr. David Livingstone. She died some years ago, and Dr. Peake is survived by two daughters and three sons, one of whom, Mr. H. L. Peake, is a surgeon in Kenya.

Dr. E. P. Carmody, who died at St. Leonards-on-Sea, Sussex, on September 28 at the age of 72, had a great love of the sea and ships. As a boy in the West Indies he learned to handle small sailing boats, and as time went on he became deeply interested in the problems of navigation. He was an original member of the Institute of Navigation, and some two years ago produced the Hezzanith–Carmody slide-rule, an invention intended to simplify the work of navigators. He was also responsible for the design of the dial of the Fowler nautical calculator. Ernest Patrick Carmody was born at Dulwich on March 27, 1883, the son of Professor P. Carmody, and from 1893 to 1900 was a pupil at the Queen's Royal College, Trinidad. He returned to London to enrol as a medical student at St. Bartholomew's Hospital, and qualified M.R.C.S., L.R.C.P. in 1908. After holding house appointments at the Royal Waterloo Hospital,

the City of London Hospital for Diseases of the Heart and Lungs (now the London Chest Hospital), the Walthamstow Hospital, and the Wanstead Children's Hospital, he settled in practice at Tilehurst, near Reading. On the outbreak of the first world war in 1914 he was appointed a civil surgeon at the Reading War Hospital, but in 1917 he entered the R.A.M.C. Transferring to the Royal Air Force in the following year, he served until 1920, later becoming vice-chairman of the Ministry of Pensions medical board at Reading. For his war services he was appointed M.B.E. in the 1919 Birthday Honours. In 1921 he took up an appointment as district surgeon in the Southern Rhodesian Medical Service, returning to England in 1932 to practise at St. Leonards-on-Sea, where he became honorary anaesthetist to the Buchanan Hospital. During the second world war he acted as an assistant in various parts of the country, returning to St. Leonards-on-Sea in 1945.

Dr. Adolph Sebba, formerly senior honorary assistant surgeon and director of the venereal diseases clinics at the Blackburn and East Lancashire Royal Infirmary, died in the Royal Marsden Hospital, London, on September 29 at the age of 59. Adolph Sebba's career started brilliantly at the University of Stellenbosch, South Africa, where he took the degree of B.A. in chemistry with first-class honours. He also won the Crole scholarship, a considerable academic achievement. After the first world war he came to England to study medicine at the London Hospital, and qualified M.R.C.S., L.R.C.P. in 1925. For the next four years he held appointments at his teaching hospital and at St. Paul's Hospital for Genito-urinary Diseases. He then accepted a resident surgical post at the Blackburn and East Lancashire Royal Infirmary, an appointment which, in time, led to his joining the honorary surgical staff of the hospital.

Dr. T. J. Burke writes: Adolph Sebba's untimely death has left medical circles in East Lancashire with a great sense of loss. Sebba—"Seb" to those privileged to know him intimately—never sought the limelight, he preferred to go about his work with a quiet and painstaking efficiency. A delightful companion with a sly sense of humour and a wide knowledge of many subjects, he had one abiding passion—surgery. He was always a keen advocate of the team spirit that should exist between the consultant and general practitioner, and went out of his way to encourage his general-practitioner colleagues to assist him at operations on their own cases outside the hospital. We had all hoped that his retirement to Bournemouth would have allowed him many happy and peaceful years with his beloved books. Alas, it was not to be. Sebba possessed a great artistic flair. He was an accepted authority on rare china, antique silver, period furniture, and fine paintings. His beautiful home was full of rare *objets d'art*, the sale of which in 1954 attracted buyers from all over Lancashire. He had a great love of music, and was a personal friend of Sir John Barbirolli, an association which went back to the time when they were students together in London. I shall always think of him as a gracious and kindly host, a fine surgeon, and, above all, a true friend.

Dr. M. W. Sellars writes: Adolph Sebba had a unique and remarkable personality. Of an inventive turn of mind, he designed early in his career an examining and operating cystoscope, incorporating what were at that time ingenious innovations. A new posterior urethroscope and a combined urological and operating table were further products of his fertile brain. For many years, despite the increasing demands of his hospital and private surgical practice, he remained an abstractor for the *British Journal of Urology* and of urological literature for the *American Journal of Surgery*. During his latter years in Blackburn his health became indifferent, an arthritic condition of his spine making his work progressively more difficult. Resigning his post at Blackburn in 1948, he retired to Bournemouth, hoping that the more congenial environment would enable him to renew the academic study of surgery. He was well on the way to realizing this ambition, when he was overtaken in the last six months by an incurable illness which he bore with great fortitude and courage. Mr. Sebba brought to East Lancashire a keen intellect, a thorough urological training, and a scrupulous surgical technique. If constitutionally unable to suffer fools gladly, he was nevertheless unrelenting in the demands he made on his own resources in his efforts to achieve perfection.

Dr. J. A. Sellars writes: I first met Mr. Sebba 25 years ago. This quiet, apparently easygoing person very soon on closer acquaintance proved to be a most keen critic who had obviously made a deep study of medicine in the widest sense, was gifted with an extraordinary memory, and followed every tenet to its logical conclusion. His work soon placed him well above the average provincial surgeon. When he was at work his patience was unending, and he spared no effort to reach a satisfactory result. We became very close friends and enjoyed many long discussions and arguments ending in the early hours of the morning. Sebba was not a man who tolerated incompetence; he was essentially an individualist, and State control was anathema to him. He met his end bravely.

Medico-Legal

ALLEGED SMOKE NUISANCE FROM RAILWAY

Four summonses for alleged smoke nuisance by railway engines at the Camden Motive Power Depot, London, were brought against the British Transport Commission at Clerkenwell on October 5.[1] Three summonses were brought on the information of Dr. D. H. Geffen, medical officer of health for St. Pancras, and the fourth on that of Mr. E. Winchester, the council's chief sanitary inspector, under Acts of 1845 and 1862. The magistrate, Mr. F. Powell, said that he understood the complaint was that in A.D. 1955 locomotives using coal or similar fuel emitted smoke. He made the comment that it had taken a long time to find that out. Mr. W. S. Holliday, for the informants, agreed that if a conviction was registered the British public would have to pay the fine. When the magistrate suggested that the summonses be adjourned *sine die*, Mr. Holliday said those instructing him wished him to continue. He said evidence would be given that observers saw engines emitting smoke for 15 minutes, and spoke to a foreman, who saw that the driver diminished the smoke. Mr. A. R. A. Beldam, for the defendants, pointed out that stringent regulations governed smoke emission, and that disciplinary action would be taken if undue smoke was caused, but with 40 or 50 locomotives getting up steam it could not be altogether avoided. The magistrate said some action should be taken "to get round this absurd position where one public authority prosecutes another public authority." If a driver or some other servant of the commission were charged and found responsible, then he and not the British public would pay the fine. The summonses were adjourned until October 20.

[1] *The Times*, October 6, 1955.

The Services

Colonel G. B. Mitchell-Heggs, O.B.E., T.D., R.A.M.C., T.A., has been appointed Honorary Colonel of a T.A. Unit, in succession to Colonel W. McK. H. McCullagh, D.S.O., M.C., T.D., R.A.M.C., T.A., whose tenure has expired.

Lieutenant-Colonel C. Cameron, R.A.M.C., has been awarded the Army Emergency Reserve Decoration.

Colonel R. A. Bennett, late R.A.M.C., has been appointed Honorary Physician to the Queen in succession to Major-General W. R. D. Hamilton, C.B., O.B.E., retired.

Major-General T. Young, C.B., O.B.E., late R.A.M.C., retired, has been appointed Colonel Commandant, R.A.M.C., in succession to Major-General K. A. M. Tomory, C.B., O.B.E., resigned.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **September 24** (No. 38) and corresponding week 1954.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	6	0	2	0	1	8	0	1	0	
Dysentery	450	71	192	14	1	308	35	133	8	
Encephalitis, acute	1	0		0		4	0	0	0	
Enteric fever:										
Typhoid	6	0	1	0	2	2	0	0	0	0
Paratyphoid	69	11	0	0	1 (B)	11	1	1 (B)	0	6 (B)
Food-poisoning	353	33		14		265	22		1	
Infective enteritis or diarrhoea under 2 years				29	104				18	18
Measles*	1,082	24	16	18	30	1,415	80	163	12	24
Meningococcal infection	15	0	14	1	2	21	1	5	0	
Ophthalmia neonatorum	34	2	7	0		37	2	6	0	
Pneumonia†	171	7	87	1	2	251	11	80	5	
Poliomyelitis, acute:										
Paralytic	201	20	44	6	3	49	1	22	4	3
Non-paralytic	193	44				35	3			
Puerperal fever§	204	20	11	1		212	33	9	0	
Scarlet fever	426	27	82	27	23	526	35	80	25	34
Tuberculosis:										
Respiratory	556	50	116	38		694	68	123	23	0
Non-respiratory	97	5	21	5		92	6	24	2	0
Whooping-cough	1,113	58	45	34	73	1,566	84	104	14	16

DEATHS in Great Towns	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		1	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	2		2	1	4	4	0	1	1	2
Influenza	6	0	1	0	2	4	0	0	0	0
Measles		0	1	0	0		0	0	0	0
Meningococcal infection		0	0				0	3		
Pneumonia	132	22	12	12	6	137	15	15	7	5
Poliomyelitis, acute	7	0	4		0	2	0	1		0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	56	4	9	2	1	63	8	5	3	5
Non-respiratory		1	1	0	2		1	6	0	1
Whooping-cough	0	0	0	0		1	0	0	0	0
Deaths 0–1 year	185	23	22	8	9	192	24	25	11	15
Deaths (excluding stillbirths)	4,582	677	490	91	146	4,673	680	542	110	178
LIVE BIRTHS	7,145	1088	835	245	419	7,249	1066	861	181	444
STILLBIRTHS	204	25	22			209	23	24		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Poliomyelitis

The number of paralytic cases notified in England and Wales in the week ending October 1 again rose slightly. The figures, with those for the previous week in parentheses, were: paralytic 207 (201), non-paralytic 180 (193), total 387 (394). Deaths in the great towns numbered 8. Notifications from the beginning of the year up to October 1 numbered 4,638; in 1947 and 1950 they were more numerous—namely, 6,666, and 6,365 respectively.

A slight increase of incidence occurred in the northern, north-western, midland, eastern, and southern regions, and the East and West Ridings of Yorkshire. The incidence decreased in the north midland, London and south-eastern, and south-western regions, and in Wales. The following districts have had particularly high rates to date (figures are for cases notified up to October 1, with rates per 100,000 of the population in parentheses): Barnsley C.B. 77 (102.9); Mexborough U.D. 18 (94.6); Willesden M.B. 154 (86.8); Hoyland Nether U.D. 13 (81.9); Wombwell U.D. 13 (69.2); Cheshunt U.D. 16 (63.1); Dover M.B. 19 (55.8); Stepney M.B. 53 (56.2); Poplar M.B. 39 (54.4); Clacton U.D. 13 (53.9).

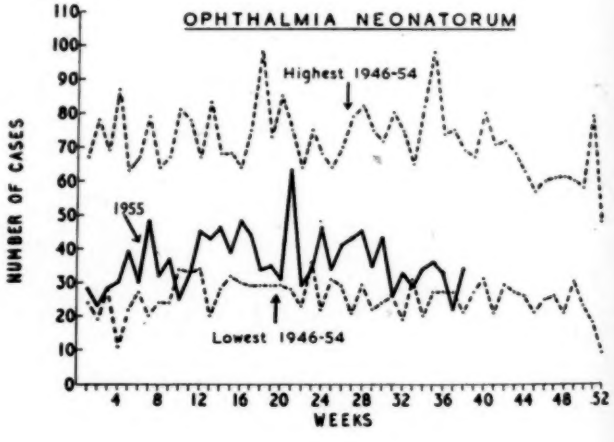
In Scotland 48 cases were notified, 4 more than in the previous week. 30 of them were reported from Glasgow, 3 more than in the previous week.

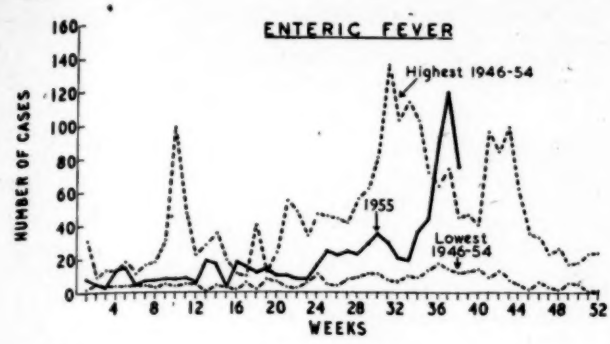
Eire in Second Quarter

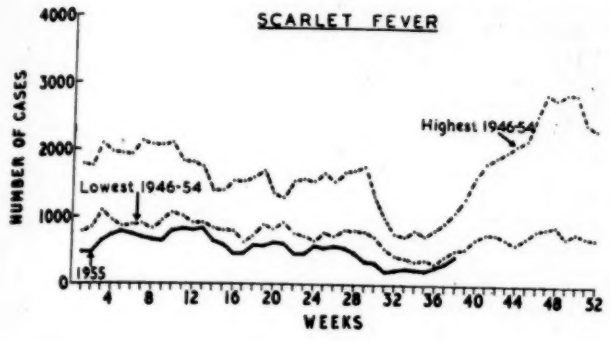
The birth rate during the June quarter of 1955 was 22.9 per 1,000 population, and was 0.9 above the rate for the preceding second quarter. The infant mortality was 36 per 1,000 registered births and the neonatal mortality was 23; for the June quarter of 1954 the infant mortality was 36 and the neonatal mortality was 21. The general death rate was 13.3 per 1,000 population, being 1.2 above the rate for the second quarter of 1954. The death rate from respiratory tuberculosis was 27 per 100,000 and for other forms 5; the rates for the second quarter of 1954 were 32 and 8 respectively. The number of deaths attributed to the principal infectious diseases included 252 from influenza, 32 from gastro-enteritis (under 2 years), 7 from whooping-cough, 5 from measles, and 3 from diphtheria.

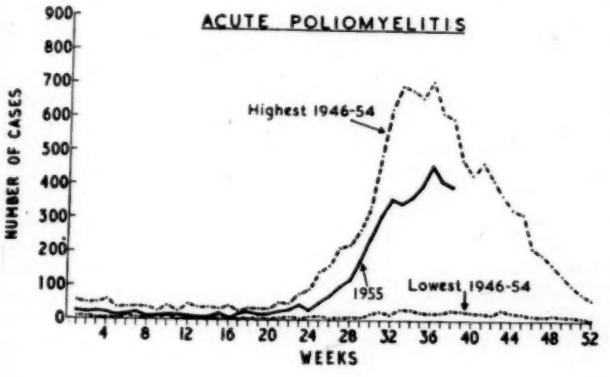
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1946–54 are shown thus ------, the figures for 1955 thus ———. Except for the curves showing notifications in 1955, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

In England and Wales during the week ending September 24 the largest rises in the number of notifications of infectious diseases were 97 for scarlet fever, from 329 to 426, 44 for measles, from 1,038 to 1,082, and 33 for dysentery, from 417 to 450, and the largest falls were 46 for paratyphoid fever, from 115 to 69, and 29 for whooping-cough, from 1,142 to 1,113.

The largest fluctuations in the incidence of measles were rises of 48 in Caernarvonshire, from 4 to 52, 37 in Monmouthshire, from 35 to 72, and falls of 50 in Yorkshire West Riding, from 81 to 31, and 31 in Devonshire, from 74 to 43. The largest rise in the returns for scarlet fever was 25 in Lancashire, from 70 to 95. The largest decline in whooping-cough was 33 in Lancashire, from 152 to 119. 6 cases of diphtheria, 3 fewer than in the preceding week, were notified. 4 of the 6 cases were notified in Lancashire (Liverpool C.B. 3).

The largest returns of paratyphoid fever were Nottinghamshire 38 (Mansfield M.B. 21, Kirkby-in-Ashfield U.D. 10, Nottingham C.B. 3, Worksop M.B. 3) and London 11 (Hackney 7). During the past four weeks a total of 155 cases have been notified in Nottinghamshire and 57 cases in London.

The largest centres of dysentery were Lancashire 138 (Blackpool C.B. 34, Liverpool C.B. 33, Haslingden M.B. 24, Manchester C.B. 12), London 71 (Chelsea 18, Southwark 13, Islington 9), Yorkshire West Riding 65 (Huddersfield C.B. 21, Leeds C.B. 17), Durham 22, and Leicestershire 18 (Leicester C.B. 15).

In Scotland the number of notifications of dysentery declined by 75, from 267 to 192; in Glasgow the fall was 59, from 169 to 110.

Week Ending October 1

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 550, whooping-cough 993, diphtheria 10, measles 1,227, acute pneumonia 228, acute poliomyelitis 387, dysentery 427, paratyphoid fever 45, and typhoid fever 5.

Medical News

Wellcome Trust.—Announcing plans for the extension of the Wellcome Trust's work, Sir Henry Dale, O.M., F.R.S., last week explained that in future the Trust would more actively seek openings for its charitable support. He introduced Dr. F. H. K. Green, formerly of the Medical Research Council headquarters, and now appointed to the newly created post of scientific secretary to the Trust. In the past the trustees' policy had had a certain "opportunist" character, said Sir Henry, and they had in general responded to appeals made to them rather than initiated a planned policy of spending. A whole-time administrative staff was now needed, and Dr. Green would have the chief executive responsibility of carrying out the Trust's policy. The trustees were contemplating some help for research in anaesthesia, and would continue to pay special attention to the needs of pharmacology and therapeutics (particularly in tropical medicine). They were also considering the establishment of more research fellowships, not for postgraduate students, who were already well catered for, but for senior men. Among the more notable of the Trust's benefactions to date had been the endowment of a chair of tropical medicine and a chair of pharmacology in London University. It had also contributed about £100,000 each to enable the library of the Royal Society of Medicine and the museum of the Royal College of Surgeons to expand. Sir Henry announced that Brigadier J. S. K. Boyd, F.R.S., was relinquishing his post as director of the Wellcome Laboratories of Tropical Medicine to become a trustee on January 1 next.

Lady Tata Memorial Trust.—On assuming the duties of Scientific Secretary of the Wellcome Trust on October 1 Dr. F. H. K. Green relinquished the secretaryship of the (European) Scientific Advisory Committee of the Lady Tata Memorial Trust, which he had held since 1934. The trustees have appointed Dr. David Galton, of the Chester Beatty Research Institute, Fulham Road, London, S.W.3, to succeed him.

Ilford Golden Jubilee.—This year the Ilford Medical Society attained its fiftieth birthday, to be celebrated by a ball on Thursday, October 20. The President is Dr. J. Arthur Moody. Ever since its formation in 1905 the Society has been active in holding clinical and social meetings, and it played a leading part in the foundation of the Ilford Emergency Hospital, now the King George Hospital. It has taken special care to foster good working relations among all sections of the profession, and maintains close and friendly contact with the B.M.A. Division. Latterly the question of continued education for general practitioners at the local hospital has been under review with the local faculty of the College of General Practitioners.

"Public Health."—The journal of the Society of Medical Officers of Health, *Public Health*, appears this month in a new guise. The cover is now light green in colour and bears the minimum of printed matter, with no advertisements. The lay-out has been improved, a better-quality paper used, and a new type-face chosen. All these changes combine to make the journal more attractive and therefore more readable. The purposes of the journal are to express the policies and views of the Society, to give members prompt news of the activities of the Society, and to publish papers on

subjects connected with public health. The October issue contains Dr. Charles F. White's presidential address to the Society, and there are other articles on handicapped adults (by Dr. J. B. Meredith Davies), on old people (by Dr. Jeanette Diamond), and on heart murmurs in children (by Dr. A. P. M. Page). During the 65 years of its existence *Public Health* has seen many changes. There have been nine editors in all. In 1936 Mr. G. L. C. Elliston took over the editorship from Dr. Charles Porter, and, apart from the period of the war, he has continued to edit the journal up to the present time. But his commitments do not now allow him to undertake sole editorial responsibility, and the Council of the Society has set up an editorial board of five, with the addition of an as yet unspecified number of corresponding members. Mr. Elliston has agreed to join the board, and he and the four other principal members will be the active editors.

British Medical Bulletin.—Number three of the eleventh volume of this well-known publication is devoted to the "Surgery of the Heart and Thoracic Blood Vessels." It is published by the Medical Department of the British Council, 65, Davies Street, London, W.1, and the current number can be obtained on application there or from a local bookseller, the price, post free, being 15s. The subject is dealt with most comprehensively under the guidance of Sir Russell Brock, chairman of the committee planning the symposium, and Mr. N. R. Barrett, scientific editor. As Sir Russell points out in his introduction, surgery of the heart and great vessels is such a recent and rapid development that it is in danger of being wrongly appraised. The current number of the *Bulletin* is a successful and notable attempt to provide a basis for such appraisement, including, as it does, articles on the surgical treatment of pulmonary stenosis, septal defects, coarctation, persistent ductus arteriosus, and valvular disease of the heart, and articles on anaesthesia for cardiac surgery, on hypothermia, cardiac resuscitation, and arterial reconstruction. The symposium is well illustrated and constitutes a valuable contribution to the subject.

Doctor Wanted for Expedition.—The British East Greenland Expedition, 1956–7, needs a medical officer. A full-scale scientific programme is planned, and the expedition plans to be away for 13 to 14 months. The medical officer will have opportunity for research. Full details from the Rev. Keith C. Treacher, 24, Brookland Hill, London, N.W.11.

Christmas Seals.—The Duchess of Portland will open the Christmas seal sale of the National Association for the Prevention of Tuberculosis on Tuesday, October 18. The seals are in different designs, and each complete sheet forms a Christmas tree. The whole sheet of 100 seals costs 4s. These, and Christmas cards in a similar design at 5s. a dozen (with envelopes), can be obtained from the Duchess of Portland, chairman, N.A.P.T., Tavistock House North, London, W.C.1, on or after October 18. N.A.P.T. is a purely voluntary body, largely financed by the Christmas seal campaign.

The National Association for Mental Health plans to open Parnham House, Beaminster, Dorset, as a home for old ladies suffering from a mild degree of mental infirmity. The object of the scheme is to prevent the unnecessary admission of such people to mental hospitals. A night and day nursing staff is provided under medical supervision. Terms are from six to ten guineas weekly. All inquiries to: The Secretary, Residential Services Department, The National Association for Mental Health, 39, Queen Anne Street, London, W.1.

The Institute of Biology has now moved from Tavistock House South to 41, Queen's Gate, London, S.W.7.

Sir Lionel Whitby has been reappointed a deputy vice-chancellor of Cambridge University for the year 1955–6. He was vice-chancellor for the two-year period 1951–3.

Dr. M. Roth has been appointed Professor of Psychological Medicine at Durham University from January 1 next in succession to Professor Alexander Kennedy, who, as previously announced, becomes Professor of Psychiatry at Edinburgh. Dr. Roth qualified at St. Mary's Hospital in 1941, and is at present Director of Clinical Research at the Graylingwell Hospital, Chichester.

New M.R.C. Members.—The Committee of Privy Council for Medical Research, after consultation with the Medical Research Council and the President of the Royal Society, has appointed the following new members of the Medical Research Council: Professor R. C. Garry, Regius Professor of Physiology in the University of Glasgow, and Mr. H. J. Seddon, Director of Studies at the Institute of Orthopaedics, British Postgraduate Medical Federation.

Dr. Louis H. Bauer.—During the Australasian Medical Congress held in Sydney in August the honorary degree of Doctor of Science of the University of Sydney was conferred on Dr. Louis H. Bauer, secretary-general of the World Medical Association. Dr. Bauer trained at the Harvard Medical School, served as a lieutenant-colonel in the Medical Corps of the United States Army, and later practised as a cardiologist. He was successively chairman of the board of trustees, president-elect, and president of the American Medical Association. Among his many other activities he founded the *Journal of Aviation Medicine*.

Dr. A. Trevor Jones has been appointed Provost of the Welsh National School of Medicine in succession to the late Dr. R. M. F. Picken.

Surgeon Rear-Admiral R. C. May becomes Surgeon Vice-Admiral and Medical Director-General of the Navy from April 30, 1956. He succeeds Surgeon Vice-Admiral Sir Alexander Ingleby-Mackenzie.

Smoke Abatement.—New appointments recently made by the National Smoke Abatement Society include Dr. W. R. Martine, senior administrative medical officer at Birmingham, as vice-president, and Dr. J. S. G. Burnett, medical officer of health at Preston, as deputy chairman of the executive council.

COMING EVENTS

Future in Africa.—An exhibition on "The Future in Africa" will be held in St. Matthew's Hall, Hereford Street, Bethnal Green, London, on October 18–22 by three main missionary societies working in Africa. Medical as well as other work will be illustrated.

Courses for General Practitioners.—Cambridge University Medical School will hold postgraduate courses for general medical practitioners in the form of one-day symposia on Saturdays during the academic year 1955–6. Each symposium will start at 10.30 a.m. and end at 4.30–5 p.m. It will consist of three to five lecture-discussions and demonstrations either of clinical cases or to illustrate modern methods. The subject matter and clinical material will be chosen for its special appeal to those engaged in general practice. Further information from the Secretary, The Medical School, Tennis Court Road, Cambridge.

St. Thomas's Hospital old students' dinner at Royal College of Surgeons, Lincoln's Inn Fields, November 10, 7 for 7.30 p.m. Details from honorary secretaries of dinner, St. Thomas's Hospital Medical School, London, S.E.1.

Leeds University Dinner.—Annual dinner of past and present men medical students at Hotel Metropole, Leeds, November 25, 7.30 p.m. Details from J. Dowson, School of Medicine, The University, Leeds, 2.

Society of Apothecaries of London.—The annual Master's Day Service of the Society of Apothecaries will be held on Sunday, October 23, at 11.15 a.m. at the Church of St. Mary Aldermary, London, E.C.1 (opposite Mansion House Station).

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, October 17

EDINBURGH UNIVERSITY.—At Anatomy Lecture Theatre, University New Buildings, 5 p.m., Eleventh Sharpey-Schafer Memorial Lecture by Professor R. A. McCance, F.R.S.: Chemical Structure of the Body.

●HUNTERIAN SOCIETY.—At Talbot Restaurant, E.C., 7 for 7.30 p.m., first dinner meeting. 8.30 p.m., Presidential Address by Mr. A. Dickson Wright: How Patients Have Deceived Me.

INSTITUTE OF NEUROLOGY.—5 p.m., Dr. Leonard Kurland (U.S.A.): Aetiological Significance of Epidemiological Research in Multiple Sclerosis and Amyotrophic Lateral Sclerosis.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—3 p.m., Mr. H. J. Fisher: Post-operative Electrolyte Balance.

INSTITUTE OF PSYCHIATRY.—5.30 p.m., Dr. E. Stengel: postgraduate lecture-demonstration.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5 p.m., Heath Clark Lecture by Mme. Alva Myrdal (Unesco): Role of Health and Education in the Process of Social Development (with special reference to underdeveloped countries)—Interplay of Factors in the Development Process.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. W. A. Briscoe: Why Do Respiratory Function Tests?

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. C. W. Flemming: Surgery in the Treatment of Osteoarthritis of the Hip—a Review of the Methods; 6.30 p.m., Professor Ian Aird: Blood Groups and Disease.

ROYAL SOCIETY OF HEALTH.—At Caxton Hall, S.W., 2.30 p.m., London Sessional Meeting. Discussion to be opened by Sir Hugh Beaver and Dr. J. A. Scott: The Clean Air Bill.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF PHARMACOLOGY.—At Physiology Theatre, 5.30 p.m., Professor J. F. Danielli, Ph.D.: Nuclear and Cytoplasmic Sites of Drug Action.

Tuesday, October 18

DEAF CHILDREN'S SOCIETY.—At Royal College of Surgeons of England, 7.30 p.m., Mr. I. G. Robin and Mr. J. C. Ballantyne: Medical Aspects of Hearing and Deafness.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. P. F. Borrie: Vascular Naevi.

●INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. Macdonald Critchley: Psychological Aspects of Pain.

LONDON HOSPITAL MEDICAL COLLEGE.—At Bearsted Theatre, 5 p.m., Schorstein Memorial Lecture by Professor L. J. Witts: Anaemia and the Alimentary Tract.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5 p.m., Heath Clark Lecture by Mme. Alva Myrdal (Unesco): Role of Health and Education in the Process of Social Development (with special reference to underdeveloped countries)—Role of Education.

●OXFORD UNIVERSITY MEDICAL SOCIETY.—At Radcliffe Infirmary, 8.15 p.m., Dr. E. E. Pochin: Speed of the Thyroid.

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Dr. H. A. Burt: Management of Minor Joint Complaints.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—3.45 p.m., Erasmus Wilson Demonstration by Dr. L. W. Proger: Pneumatosis.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. J. B. Pennybacker: Pituitary Tumours; 6.30 p.m., Professor W. W. Mushin: Anaesthetic Emergencies.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—5 p.m., Bengué Memorial Award Lecture by Professor G. P. Crowden: Environmental Factors Affecting Comfort, Health, and Working Capacity (illustrated).

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Theatre, 5 p.m., Mr. A. C. H. Bell: Management of the 3rd Stage of Labour and Postpartum Haemorrhage.

SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, 8.30 p.m., Dr. Mary J. Wilmers: Allergic Diseases of Children.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. J. Minton: Ocular Manifestations in Clinical Neurology (Part I).

Wednesday, October 19

COLLEGE OF GENERAL PRACTITIONERS.—At Ronkswood Hospital, 3.30 p.m., Mr. J. A. Chalmers: Bleeding at the Menopause.

EUGENICS SOCIETY.—At Royal Society, Burlington House, W., 5.30 p.m., Dr. J. F. Loutit: Biological Hazards of Nuclear Fission.

HYPNOTHERAPY GROUP.—At Royal Society of Medicine, 8 p.m., Dr. A. G. Davies: Scope and Limitations of Hypnotherapy.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Mesenchymal Tumours of the Corium.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. T. Holmes Sellors: Diaphragmatic Hernia.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. J. G. Sandrey: Urological Emergencies in General Practice.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5 p.m., Heath Clark Lecture by Mme. Alva Myrdal (Unesco): Role of Health and Education in the Process of Social Development (with special reference to underdeveloped countries)—Enigma of Health Progress.

MIDLAND MEDICAL SOCIETY.—At Midland Hotel, Sir Ernest Finch: Leonardo da Vinci.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. J. D. N. Nabarro: Diabetes and Carbohydrate Metabolism.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH.—3.30 p.m., Sir Clement Price Thomas: Conservative Resection of the Bronchial Tree.

ST. MARYLEBONE HOSPITAL FOR PSYCHIATRY AND CHILD GUIDANCE.—5.30 p.m., Dr. E. H. Larkin: Major Psychiatric Syndromes.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF EUGENICS, BIOMETRY AND GENETICS.—At Anatomy Theatre, 5.45 p.m., Galton Lecture by Dr. J. V. Neel (Michigan): Genetic Control of Haemoglobin Synthesis.

WILLESDEN GENERAL HOSPITAL MEDICAL SOCIETY.—At Department of Physical Medicine, Willesden General Hospital, 8.45 p.m., Mr. T. I. Hughes: Post-hysterectomy Problems.

Thursday, October 20

BRITISH INSTITUTE OF RADIOLOGY.—8 p.m., Mr. E. Cotchin: Neoplasia in Domesticated Mammals.

GLASGOW UNIVERSITY MEDICO-CHIRURGICAL SOCIETY.—7.30 p.m., Dr. J. A. Imrie: Forensic Problems.

ILFORD MEDICAL SOCIETY.—At Royal College of Surgeons of England, Golden Jubilee Ball.

LIVERPOOL MEDICAL INSTITUTION.—8 p.m., Symposium: Hiatus Hernia. Openers, Mr. F. Ronald Edwards and Professor C. A. Wells.

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Royal Free Hospital School of Medicine, 8.30 p.m., Rev. J. Wilson, Dr. Clara Stewart, and Dr. C. M. Billington: Influence of the Spiritual Factor in Healing.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—8.30 p.m., clinical meeting.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5 p.m., Heath Clark Lecture by Mme. Alva Myrdal (Unesco): Role of Health and Education in the Process of Social Development (with special reference to underdeveloped countries)—Systematic Improvement of Human Resources Through Health and Educational Measures.

MANCHESTER MEDICAL SOCIETY.—At Manchester University, 8 p.m., Section of Anaesthetics. Dr. J. McAuley: Two Schools of Thought.

ROYAL EYE HOSPITAL.—5.15 p.m., Dr. T. H. Whittington: Aspects of Refraction—II. Introduction to Binocular Vision and its Investigation.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—7.30 p.m., Presidential Address by Professor R. M. Gordon: Host-Parasite Relationship in Filariasis.

ST. ANDREWS UNIVERSITY.—At Physiology Department, Queen's College, Dundee, 5 p.m., Professor R. A. McCance, F.R.S.: Metabolism and Renal Function in the First Two Days of Life.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. D. J. Williams: postgraduate demonstration in neurology.

●WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At Fellows' Restaurant, Zoological Gardens, 7.15 for 7.30 p.m., dinner meeting. 9 p.m., Presidential Address: Man Alive.

Friday, October 21

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, 5 p.m., Radiotherapy Section Meeting. Dr. E. F. Scowen: Indications for the Ablation of Endocrine Activity in the Ovaries, Adrenals, and Anterior Pituitary in the Treatment of Breast Cancer.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. R. T. Brain: Naevi.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. L. Livingstone: clinical demonstration.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—3.30 p.m., Mr. W. S. McKenzie: Tonsil and Adenoid Problem.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—3 p.m., Professor R. J. Kellar: Placental Dysfunction.

KENT AND CANTERBURY HOSPITAL.—8 p.m., clinical meeting.

LONDON UNIVERSITY.—(1) At London School of Hygiene and Tropical Medicine, 5 p.m., Heath Clark Lecture by Mme. Alva Myrdal (Unesco): Role of Health and Education in the Process of Social Development (with special reference to underdeveloped countries)—Social Action and Social Research. (2) At Anatomy Theatre, University College, 5 p.m., special university lecture in human anatomy and morphology by Dr. R. W. Sperry (California): Some Neural Mechanisms Underlying Perception.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—(1) 2 p.m., Mr. S. M. Cohen: Management of Limb Gangrene; (2) 4 p.m., Professor W. D. M. Paton: Application of Synaptic Pharmacology to Clinical Practice.

SIGERIST SOCIETY.—At 45, Russell Square, W.C., 7.30 p.m., Dr. B. H. Kirman: Problem of the Backward Child.

Saturday, October 22

BIOCHEMICAL SOCIETY.—At Department of Physiology, Bedford College, Regent's Park, N.W., 2 p.m., scientific papers.

KENT PAEDIATRIC AND CHILD HEALTH SOCIETY.—At Farnborough Hospital, 3 p.m., Dr. G. Brownlee: Antibiotics.

WEST MIDLAND PHYSICIANS ASSOCIATION.—At Queen Elizabeth Hospital, Birmingham, 11 a.m., autumn meeting.

APPOINTMENTS

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—R. H. C. Robins, M.B., B.Chir., F.R.C.S., Senior Orthopaedic Registrar to Exeter Clinical Area; A. A. Reid, M.B., B.S., M.R.C.P., D.P.M., Senior Psychiatric Registrar at Moorhaven Hospital, Ivybridge, South Devon; R. H. R. White, M.B., B.Chir., M.R.C.P., D.C.H., Medical Registrar to St. Martin's Hospital and the Royal National Hospital for Rheumatic Diseases, Bath; R. L. Bishton, M.D., Consultant Pathologist to Bath Clinical Area; P. K. Ganguli, M.B., B.S., D.M.R.D., D.M.R.T., Senior Registrar in Radiodiagnosis to Southmead and Frenchay Hospitals, Bristol; J. H. Hodgson, M.B., B.S., Surgical Registrar to the Bath Group of Hospitals; L. Dawson, M.B., Ch.B., Registrar in Diseases of the Chest, Bristol Chest Clinic and associated hospitals.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Fleck.—On September 27, 1955, at Hillingdon Hospital, to Joy, wife of Dr. D. G. Fleck, a daughter—Suzanne Lesley.

Greenberg.—On September 29, 1955, at Rush Green Hospital, Romford, Essex, to Leila (formerly Gordon), wife of R. C. Greenberg, M.B., B.S., D.P.H., a second son—Roger Keith.

Kirk.—On September 16, 1955, at Queen Charlotte's Hospital, London, W., to Dr. and Mrs. R. M. Kirk (Dr. Margaret Schafran), a daughter—Valentine Moya.

MARRIAGES

Flynn—Warrick.—On September 24, 1955, at St. John's, Blackheath, London, S.E., Frederick Flynn, M.D., to Ann Warrick, M.B., B.S., D.C.H.

O'Reilly—Daley.—On October 8, 1955, at Wimbledon, London, S.W., J. N. O'Reilly, M.R.C.P., to Doreen Daley, F.R.C.O.G., daughter of Sir Allen Daley, F.R.C.P., and Lady Daley.

DEATHS

Bradshaw.—On September 14, 1955, Gerald Arthur Bradshaw, M.R.C.S., L.R.C.P., D.O.M.S., of 12, Wycombe Gardens, London, N.W.

Clark.—On September 13, 1955, Alexander Erskine Clark, M.B., Ch.B., of Hawkstone House, Fareham, Hants, aged 73.

Crawford.—On September 16, 1955, at 37, Royal Avenue, Scarborough, Yorks, David Kenneth Crawford, M.B., F.R.C.S.Ed., late of Berkhamsted, Herts.

Davison.—On September 1, 1955, at Northampton General Hospital, Thomas Reginald Davison, M.B., B.S., D.Obst.R.C.O.G., of Linhope Lynn, Queen's Park Parade, Northampton.

Wilson.—On August 18, 1955, at 97, Remuera Road, Auckland, New Zealand, Harold William Wilson, M.D., F.R.A.C.P.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Motor Fuels and the Hazard to Tractor Drivers

Q.—*What is thought to be the long-term toxicity of fumes from motors using petrol or diesel oils? If such fumes are harmful, are they likely to be inhaled by a tractor driver in the open air? In many tractors the exhaust pipe is just in front of the driver.*

A.—While petrol has been in general use for internal combustion engines for about fifty years, diesel oil has been extensively used only during and since the last world war, and in Britain farm tractors have been increasingly used during the same period. This corresponds with the period of increasing lung cancer incidence. All these fluid fuels are incompletely oxidized under normal running conditions, and among the products of combustion are sulphur dioxide, carbon monoxide, nitrogen, and many hydrocarbons. Some of the latter are polycyclic hydrocarbons, and notably 3:4-benzpyrene is a potent carcinogen for many animals.

Extensive work has been done on exhaust fumes, particularly by Kotin in Los Angeles, where the concentration of automobiles is high and where local geographical conditions favour stagnation of the atmosphere and consequently the persistence of smog. Both petrol and diesel fumes are present in this smog, and 3:4-benzpyrene has been identified in both types of fumes by several independent groups of investigators in different parts of the world. A survey of the present position, and recommendations for improvements, are contained in the Report of the Committee on Air Pollution, 1954 (see *Journal*, December 4, 1954, p. 1340).

The design of tractors seems to leave room for improvement. Undoubtedly drivers must inhale some of the exhaust fumes, even though working in the open air. How far inhalation of such fumes may lead to an increased incidence of lung cancer is not yet known, but the fumes are certainly potentially harmful as well as unpleasant. In large urban communities the presence of many buses and lorries with diesel engines constitutes an increasing nuisance, if not a definite health hazard. The emission of excessive smoke by a vehicle is illegal in Britain, but the law is rarely enforced.

Pruritus in the Elderly

Q.—*I often see elderly patients who complain of itching of the skin, yet on examination no skin lesion is visible. Is this an atrophic condition, and what line of treatment is indicated?*

A.—Itching is often an important early symptom of general disease. The causes of itching in the elderly are varied as at all other ages, but do not include an atrophic condition of the skin. It is important to exclude such underlying general medical causes as malignant disease, diabetes, renal disease, blood dyscrasias, nutritional deficiencies, and vascular degenerations. The latter may affect the peripheral circulation, and itching in elderly patients often involves chiefly the extremities and is especially troublesome in the winter. Vascular disease may sometimes cause itching from central nervous degeneration. As at other ages, emotional disturbances may be responsible for itching in the elderly, and even parasites must not be overlooked. A winter itch may sometimes be due to intolerance of winter underwear. On the other hand, itching may precede the clinical signs of such diseases as lichen planus, pemphigus, or reticuloses by a considerable interval. There remain a number of cases without obvious explanation, and treatment has to be symtomatic or empirical. Some of these may depend upon endocrine influences, but not of an order to make treatment rational.

Where simple general and local measures fail to give relief a few empirical remedies are worthy of trial. Amphetamine, usually in a dose of 5 mg. daily, is sometimes effective if there is depression of which the pruritus may be a symptom and not the cause. Methyltestosterone, 5 mg. twice or thrice daily, is also occasionally helpful. Cortisone in small doses, 25 mg. two or three times a day, is often of value, as is hydrocortisone ointment. Locally relief may attend the use of *x* rays or Grenz rays, high-frequency current, or the gentle brushing of the skin with a soft hairbrush.

"Calgon" and Hypodermic Syringes

Q.—*Where I live the water is particularly hard, and the constant boiling of all-glass syringes is gradually rendering them useless because of the deposition of fur upon barrels and plungers. The possibility of using "calgon" (sodium hexametaphosphate), a commercial water-softening agent, has been considered. Is it known whether this chemical has any deleterious effect on penicillin, or whether such traces as may remain in the syringe are at all harmful when introduced into the body parenterally?*

A.—Calgon has not only no deleterious effect on penicillin but Dr. Lester Smith showed several years ago that calgon would stabilize solutions of penicillin. Calgon is certainly not toxic in the traces which would remain in a syringe. It is said that waterworks companies have sometimes added it to water.

Changing Malaria Prophylactic

Q.—*A non-immune person in an area chiefly infested with M.T. malaria wishes to change from one prophylactic to another. How should the transition be managed (a) after a successfully treated attack of malaria, (b) with no intervening attack? Are any special precautions indicated during the transition?*

A.—There are no special precautions to be observed when changing malarial prophylactics. The patient merely discontinues taking one and commences to take the other in appropriate amounts and at suitable intervals of time, both of which vary with different drugs. Similar considerations apply after an attack of malaria; the prophylactic regime should be adopted as soon as administration of the drug used in treatment has been discontinued.

Headache in Hypertension

Q.—*What is the best treatment for headache in hypertensive patients? I have found ergotamine tartrate very good. Is this effect well recognized? What part does posture play in the production of the morning headache that is so frequent a symptom?*

A.—Headache in hypertension may be of three types: (1) A vague variable "tension" headache related to an accompanying anxiety state. (2) Migraine headaches may become exaggerated or reappear when hypertension develops. (3) There may be an intense, severe, and crippling true hypertensive headache, often accompanied by giddiness, pain down the back of the neck, etc., and which on occasions may precede encephalopathic seizures.

The treatment varies. The first type will respond to phenobarbitone or aspirin; the second to ergotamine. In the third type—the real hypertensive headache—a good response is obtained by the use of hypotensive agents. A subcutaneous injection of an *effective* dose of pentolinium at night will nearly always prevent these severe morning headaches.

The mechanism of the morning headache is not understood: its relation to posture is well known to the patients, who know that it will not pass off unless they struggle to their feet. Vascular disturbances in the meninges are generally believed to cause headaches. The autonomic regulatory changes occurring at the end of a night's rest are probably responsible for some changes in meningeal vascular calibre

which trigger off the headache. The relief produced by appropriate doses of ganglionic blocking agents is compatible with such a view.

Psychogenic Respiratory Arrhythmia

Q.—*Can you suggest any treatment for a male schoolmaster, aged 54, who is woken up at night, when in full expiration, with the feeling that he cannot get his breath? The attacks last only a few seconds, but the feeling of suffocation wakes him up, and he can do nothing to get his breath back while they last. He says his sister has the same trouble. He does not suffer from asthma.*

A.—By far the most likely explanation for the attacks that the patient and his sister experience, in the absence of hypertension or asthma, is a respiratory arrhythmia of psychogenic origin. Such attacks are not uncommon and are akin to the sudden terror attacks which some patients experience at night. It is generally assumed that they are connected with some dream-like state of nightmare quality, and they come most frequently just as the patient is falling off to sleep.

Explanation, reassurance, and a moderately powerful hypnotic at night may lead to symptomatic relief, but the symptom may point to the necessity for more formal psychotherapy.

Urinary Calculus in the Tropics

Q.—*Is there any recognized dietary reason for the increased prevalence of vesical (and renal) calculus in the Tropics? Are there reasonable precautions that people resident in such areas should be advised to take? Some amongst the indigenous population assert that hard water is dangerous and will only drink rain water; is this correct?*

A.—The increased prevalence of renal calculi in the Tropics is almost certainly due not to the mineral constituents of water drunk but to the passage of concentrated urine caused by dehydration resulting from climatic conditions. In regions in which schistosomiasis is endemic this also predisposes to the formation of urinary calculi.

Apart from taking standard prophylactic measures against schistosomiasis, the remedy lies in drinking sufficient water to prevent the urine becoming concentrated and highly coloured. It does not matter whether the water drunk is hard or soft; the amount drunk is the only important factor. Mineral ingested in drinking water is in any case much less than that contained in the remainder of the diet.

Probenicid in Gout

Q.—*Is probenicid suitable to use in the domiciliary treatment of gout? If so, please give details of its administration and dangers.*

A.—Probenicid is a potent uricosuric agent, increased uric acid excretion in the urine being most marked on its first administration to a patient with a high blood uric-acid level. It is important, therefore, to maintain a large fluid intake and keep the urine alkaline to prevent deposition of crystals of uric acid in the renal tract. Toxic effects are uncommon and mild; occasional nausea, dyspepsia, and drug rash have all been observed, but can usually be controlled by reducing the dose. Not uncommonly acute attacks of gout occur during the first two weeks of administration, but the likelihood of this complication can be reduced by giving small doses to begin with, and by the routine use of colchicine—for example, tab. colchicin., *B.P.*, gr. 1/120 (0.54 mg.), twice daily during the first two weeks of administration. A simple procedure is to give one tablet of probenicid (0.5 g.) daily for one week, two tablets daily for a further week, and thereafter three tablets a day. The blood uric-acid level rapidly falls to about 60% of pre-treatment values. Probenicid should be given continuously once embarked upon, for discontinuation will be followed by a rising blood uric acid to previous levels. By prolonged therapy it is believed that the frequency and severity of acute attacks can be diminished, but the most important effect is in the reduction or even prevention of tophaceous deposits. It is of no value in the treatment of the individual acute paroxysm, which requires treatment with colchicine, etc., in the usual manner. Biochemical control of the effect of probenicid is of course advantageous and can best be achieved by hospitalization during early therapy, but where this is not possible there is no contraindication to the use of probenicid in the home from the beginning.

Intention Tremor in Disseminated Sclerosis

Q.—*How are the intention tremors of disseminated sclerosis accounted for? How is their almost complete disappearance during a remission explained?*

A.—The intention tremors of disseminated sclerosis are caused by lesions involving the cerebellum or its connexions. The disappearance of this symptom, as of other symptoms in the disease, in a remission is due to recovery of function in surviving axons.

Preservation of Books in the Tropics

Q.—*Will you please tell me how I can prevent books from being attacked by insects and especially by fungus in the Tropics? The warmth and moisture are very conducive to the multiplication of fungus, which forms pale patches on book covers.*

A.—A safe and effective fungicide to apply to book covers is a 2% solution of sodium pentachlorphenate in water, applied with a soft brush. If unobtainable, sodium benzoate could be substituted for the above fungicide. Fresh attacks should be prevented by this treatment, but damage done by old attacks may still show. The fungicidal solution should at first be applied to a small part of the cover in an inconspicuous place to make sure that the fabric is not disfigured by the treatment. With leather-bound books, a 1% solution of copper oleate in paraffin oil is a useful protective.

The insect attacks are probably upon the glue in the backing of the books, although insects which attack leather and those which eat fungi growing in damp cupboards may be present at times. A 5% dicophane (D.D.T.) dust should be blown down the backing of the books. On no account should the damp books be fumigated with burning sulphur.

Persistent Vulvo-vaginitis

Q.—*What are the likely causes of severe vulvo-vaginitis of six-months duration in a woman of child-bearing age? Repeated swabs have revealed only Bact. coli, non-haemolytic streptococci, and later staphylococci. Antibiotic therapy with penicillin and streptomycin and local treatment have been unavailing.*

A.—The most probable explanation of persistent inflammation affecting both vulva and vagina in the circumstances outlined is an infection with *Candida albicans*. A positive report in respect of *Bact. coli* and cocci is of no value in excluding the presence of *Candida albicans*, since its detection may call for special culture methods. Contrary to general opinion, the white patches of "thrush" are not invariably present in *Candida* infections. It is necessary to remember that persistent vaginal thrush is found particularly in patients suffering from diabetes mellitus, which has no doubt been excluded, and that many persistent inflammations of vulva and vagina are attributable to over-treatment. It is necessary to warn the patient against frequent douching of any kind, and particularly to caution against the use of strong antiseptics. These patients often have strangely morbid psychological reactions which may take the form of obsessive douching. If there is any lurking *Candida* infection there is no doubt that treatment with penicillin and streptomycin must do harm, and the same caveat must be entered in respect of other antibiotics. The severest

forms of vulvo-vaginitis seen in gynaecological out-patients at the present day are attributable to untoward reactions to oxytetracycline. Without further detail of bacteriological findings and naked-eye examination, it is not possible to be very helpful in suggesting further treatment.

Effect of Leucotomy on Endocrine Function

Q.—*What endocrinological effects may follow leucotomy, particularly changes in calcium metabolism and rarefaction of bone?*

A.—There are no generally recognized endocrinological effects of prefrontal leucotomy, though clearly injury to the hypothalamus might produce such disturbance. Of course, posteriorly placed cuts which injure the subcallosal fasciculus may give rise to trophic disturbances in the skin with oedema. Such incisions may also lead to a great diminution in spontaneous activity and joint contractures. In this type of case immobility may lead to skeletal decalcification.

Ventilation of Accumulator-Charging Rooms

Q.—*What is the present accepted practice regarding the ventilation of large accumulator-charging rooms? I interpret Section 47 of the Factories Act, 1937, as applying, in which case exhaust ventilation should be provided. However, I am told that this leads to passage of acid mist over the accumulator terminals, causing corrosion, and that ventilation by an impeller fan with air outlets at or near floor level is a better system.*

A.—It is not the usual practice to apply exhaust ventilation to accumulator-charging rooms. What is needed is good general ventilation with the air inlets low down and the exits high up in the walls to remove the hydrogen which comes off during the charging process. An extraction fan high up in the wall would assist the air movement. Though hydrogen is an explosive gas, the concentration in a battery-charging room rarely comes within the explosion range. The appropriate section of the Factories Act is therefore Section 4 and not Section 47.

The accumulator terminals are always in contact with acid, and a little more in the form of mist would not harm them.

Anodyne for Patients Dying of Lung Cancer

Q.—*Can you please tell me the prescription of the mixture usually attributed to the Brompton Hospital for use in patients with carcinoma of the lung?*

A.—The preparation used at the Brompton Hospital to relieve suffering in patients dying of carcinoma of the lung is as follows: morphine hydrochloride, ¼ gr. (16 mg.); cocaine hydrochloride, ¼ gr. (11 mg.); one drachm (3.5 ml.) each of honey and gin (alternatively, one drachm of syrup and 30 min. (1.7 ml.) of rectified spirit); chloroform water to ½ fl. oz. (14 ml.).

It is perhaps worth while pointing out that this is not the preparation commonly known as the Brompton Hospital mixture. This is a very different mixture which appears in the *National Formulary* under the heading "Mist. Sod. Chlorid. Co." and which is used as an expectorant.

Inheritance of Multiple Exostoses

Q.—*A patient suffering from multiple exostoses from infancy is doubtful about the desirability of his having children. What is known of the heredity of this complaint?*

A.—While no complete survey has yet been made, the condition of multiple exostoses is due in most, if not all, cases to a dominant gene which manifests itself in all the males and the majority of females who possess it. Accordingly, on the average about a half of the sons and rather less than half of the daughters of a man with multiple exostoses will also have the condition.

NOTES AND COMMENTS

A Good Head of Hair and Cancer.—Dr. H. Grundmann (Sheffield) writes: I was interested to read in "Any Questions?" (September 17, p. 748) the inquiry as regards the relationship of cancer and "a good head of hair." I am quite sure in my mind that the inquirer's observations are *not* coincidental. I remember quite distinctly from my student days, when in 1926 Professor H. Eppinger, then recently appointed to the Chair of Medicine at Freiburg, told us: "Beware of the middle-aged male patient with hardly a grey hair on his head: he may quite likely have, or develop, a cancer of his stomach or elsewhere." Professor Eppinger was, of course, unable to give us a rational explanation, but simply pointed it out to us as a result of clinical empiricism. I wonder whether the inquirer's cases, apart from having "a good head of hair," did also have "hardly a grey hair."

Dog Bites.—Captain R. G. Newton (B.A.O.R.) writes: May I comment on the reply given to the question on dog bites ("Any Questions?" July 16, p. 214)? Until recently many people had a dread of getting "lockjaw" from a cut between the thumb and forefinger. This fear is now replaced by a similar fear, encouraged by many doctors, including your expert, of getting tetanus from a dog bite. Yet I fail to understand why this fear is taught. Why should a dog bite be any more dangerous than a laceration or abrasion from any other potentially dirty instrument? No one seems unduly concerned at a scratch from a cat's claw, yet in my experience this is a much commoner injury; these wounds are far more likely to be soiled with earth and far more frequently become inflamed, if not definitely septic. I require far stronger evidence than "Dogs spend a good deal of time grubbing in the soil" before I shall routinely submit all my patients suffering from dog bites to the dangers and discomforts of A.T.S. injections.

Our Expert writes: There is, of course, no relevance between the two fears Dr. Newton mentions. The first of these is an old wives' tale so far as the specificity of the local wound is concerned (though I trust Dr. Newton has not forgotten that cases of tetanus have occurred from wounds at this site). The important point surely is that a wound should be treated on its merits. A dog bite is commonly deep, there may be a little crushed tissue in the depths, and these two factors favour the growth of an anaerobe. It is indisputable that the trivial puncture which is overlooked is a greater danger than the severe laceration, and that clinical tetanus nowadays most often occurs as a sequel to relatively slight injuries. It is conceivable that some cat scratches would justify the administration of A.T.S.; but, as most of them are rather superficial, there is some justification in regarding the deeper dog bite as more risky. I am not aware that any "fear" of dog bites is taught, though I do know the fact that cases of tetanus have occurred following dog bites. The management of the seemingly trivial wound is always difficult. However, when a patient presents with such an injury to the doctor it would seem a wise precaution to give A.T.S. This is not to deny the very occasional risks of giving serum, though it is presumed that the doctor would weigh this up carefully in each case.

Correction.—In the letter on barbiturate poisoning by Drs. M. S. Perinpanayagam, Grace Nicholls, and J. D. Osmond (*Journal*, October 8, p. 912), the dose of "megimide" should have been recorded as 425 mg. and not 4,250 mg.

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